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PSYCHOGENIC RHEUMATISM: THE MUSCULOSKELETAL EXPRESSION OF PSYCHONEUROSIS*

BY

EDWARD W. BOLAND

Los Angeles, California

For the development of a psychosomatic disorder there are three requisites: (1) a psychoneurotic predisposition; (2) an exciting emotional conflict, and (3) restriction of outward expression of the conflict. All individuals, whether normal or psychoneurotic, seek relief from the mental suffering occasioned by disturbing life problems. When emotional tension is expended by outward expression, muscular or verbal, all is well. By taking some form of action or doing something about it, the individual " gets it off his chest " and feels better. But if emotional dissipation is constantly restricted, the tension gradually mounts and, in a psychoneurotic type of individual especially, the development of somatic complaints may be the eventual outlet. With the emergence of bodily symptoms the psychoneurotic tends to focus his attention on them, and thereby is partially relieved from his inner mental tension. The psychophysiologic mechanism by which psychic disturbances are displaced into physical symptoms is not fully understood; undoubtedly it is complex. Recent studies suggest that emotions may affect the autonomic nervous system either directly or through the endocrine system, thereby producing increased muscle tension, vasospasm, or metabolic changes in various organs and structures.

Physicians in general are familiar with those functional symptoms or symptom complexes which are expressed in various systems, exclusive of the musculoskeletal system. The idea that structural changes in certain organs may result from psychic disturbances is also being accepted. The following is a partial list of disorders now recognized as psychosomatic: gastrointestinal system—functional dyspepsia, anorexia nervosa, irritable colon, cardiospasm, pylorospasm, certain cases of peptic ulcer and of chronic ulcerative colitis; cardiovascular system—neurocirculatory asthenia, effort syndrome, functional arrhythmias, acrocyanosis, Raynaud's disease, and certain cases of hypertension; respiratory system—certain cases of asthma, allergic rhinitis, and chronic bronchitis; genito-urinary system—enuresis, vaginismus, certain cases of impotence, and dysmenorrhoea; nervous

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system—functional headaches, migraine, hysterical anaesthesia, paraesthesia, paralysis, certain cases of epilepsy and chorea, etc.; skin—certain cases of pruritus, eczema, urticaria, and angioneurotic oedema.

Physicians are not so familiar, however, with the fact that disabilities of the locomotor system frequently result from psychic causes. Too often functional musculoskeletal symptoms are mislabelled as arthritis or some other organic disease. By failing to recognize the true nature of the complaints and by treating the patient for arthritis the physician fosters rather than alleviates the disability. Psychogenic rheumatism may be defined as the musculoskeletal expression of functional disorders, tension states, or psychoneurosis. It implies that such symptoms as pain, aching, stiffness, muscular fatigue, subjective sense of swelling, or limitation of motion may be caused, intensified, or perpetuated by mental influences. The term should be restricted for cases in which the actual disability results from functional symptoms. The usual minor nervous reactions which develop in patients with chronic arthritis should not be included unless the functional overlay grows to the point that it becomes the major incapacitating factor.

Psychogenic rheumatism does not embrace in its concept the idea that organic joint disease may result from mental conflicts. That rheumatoid arthritis may at times be a psychosomatic disease has been suggested, but most authorities agree that psychic disturbances alone cannot cause the disease. Grief, worry, or anxiety may occasionally act as precipitating agents and in some cases appear to be temporally related to fluctuations in the clinical course of rheumatoid arthritis. But while emotional upsets may act as trigger mechanisms to set off the disease process, it is probable that the body must first harbour the causative factor (infectious agent or whatever the factor is). In this sense rheumatoid arthritis cannot be considered as a psychosomatic disease. Actually in our experience, contrary to that of others (Cecil, 1945; Halliday, 1944; Patterson and others, 1943), emotional crises have seldom been related temporally to the onset of rheumatoid arthritis. In a special study (Finney, Boland, and Hench, unpublished) of possible precipitating factors in one hundred soldiers with rheumatoid arthritis an emotional upset was considered as the possible factor in only one instance, much less often than other factors (infection twelve times, physical exposure nine times, joint trauma three times, physical exhaustion twice, etc.).

Incidence

Psychogenic rheumatism must be included among the common rheumatic disorders, along with osteo-arthritis, rheumatoid arthritis, primary fibrositis, and rheumatic fever. Its incidence was appallingly high among soldiers with musculoskeletal incapacities admitted to military general hospitals and special arthritis centres. At such installations medical officers were especially on the outlook for psychogenic disorders, and the incidence of functional symptoms displayed by the muscles and joints was found to be comparable to those demonstrated by other systems, such as the gastrointestinal and cardiovascular. Psychogenic rheumatism was the most frequent cause of disability (34%) in 450 consecutive soldiers with rheumatic complaints admitted to an Army general hospital located in the United States (Boland and Corr, 1943). Previous to admission

such cases had received organic diagnoses, usually arthritis. In a general hospital located overseas Short (1947) found that one-sixth (16·5%) of 309 soldiers with articular complaints were incapacitated by psychogenic rheumatism; an incidence equalling that for osteo-arthritis and exceeded only by that for rheumatoid arthritis. Flind and Barber (1945) reported that in about 42% of patients admitted to a Royal Air Force special rheumatic centre the disability was essentially psychogenic. A statistical variance of interest was that reported by Copeman (1942) at a British general hospital in France, where emotional factors must have been plentiful; 70% of admissions were diagnosed as fibrositis, and no mention was made of functional musculoskeletal complaints. Evaluated in the light of the military experience of others, many of his cases of "fibrositis" must have been suffering from psychogenic rheumatism. At the rheumatism centres of the United States Army approximately one out of every seven soldiers was disabled because of psychogenic rheumatism. It was the second most common diagnosis at the centre at the Army and Navy General Hospital (exceeded only by rheumatoid arthritis) (Boland, Stephens, and Hench, unpublished), and the third most common at the centre at Ashburn General Hospital (being exceeded by rheumatoid arthritis and osteo-arthritis).

The incidence among civilian patients probably is almost as great as among soldiers, although as yet there are very few statistical data. Halliday (1941), working as a medical referee with the insured population of Scotland, found that 39% of 145 consecutive patients labelled as having rheumatism (including fibrositis, lumbago, sciatica, and neuritis) were incapacitated because of psychoneurosis. The incidence of "psychoneurotic rheumatism" was still greater (40 to 60%) when only those on the sick list for two months or over were considered. In a recent statistical survey of 500 consecutive private patients referred to the author because of rheumatic disease, the diagnosis of psychogenic rheumatism was made in 13·4%. Its incidence was less than that for osteo-arthritis (25%), rheumatoid arthritis (23·4%), and primary fibrositis (18·2%), but was far greater than for any of the remaining types. This series contained very few insured patients and no compensation cases.

Diagnosis and Clinical Picture

The diagnosis of psychogenic rheumatism is not made merely by excluding organic disease; positive evidence for psychoneurosis must also be established. Diagnosis depends on: (1) absence of organic disease or insufficient disease to account for the disability; (2) qualitative functional characteristics of the disability; (3) positive diagnosis of psychopathology.

Absence of Organic Disease or Insufficient Disease.—Psychogenic rheumatism may be divided conveniently into three subtypes: (1) pure—when clinical, laboratory, and radiographic evidence of organic joint disease or muscle abnormalities are lacking; (2) superimposed—when incapacitating psychogenic symptoms are associated with non-disabling organic changes; (3) residual—when disability is perpetuated due to functional symptoms which take over after the disease process itself has subsided. The relative frequency of these subdivisions (among soldiers) based on 1,021 cases of psychogenic rheumatism at the Army Rheumatism Centre, Army and Navy General Hospital, was as follows: pure, 425 (41·6%); superimposed, 404 (39·5%); residual, 192 (18·9%). A similar relative incidence probably occurs with compensation cases, but among private patients the pure type is more common.

Disabling functional complaints are superimposed most frequently on the less serious rheumatic diseases, especially primary fibrositis and osteo-arthritis, diseases which of themselves usually have nuisance value only; rarely are they superimposed

on a serious articular disease such as rheumatoid arthritis. By far the most common association both in civilian and military practice is with fibrositis. This syndrome, which rarely is incapacitating except during acute phases which do not persist indefinitely, may engender chronic invalidism in the psychoneurotic individual. The overlay of functional symptoms may be so intense that ability to carry on may be less than in patients with well-developed rheumatoid arthritis. The differentiation between psychogenic rheumatism and primary fibrositis often is not easy, and when the two conditions coexist attempts to appraise the proportion of the disability caused by each is even more difficult. Another frequent association is with osteo-arthritis. Minimal spurring in the lumbar spine or knees may be accompanied by marked and persistent disability far out of proportion to that usually seen with such changes, especially if the patient is aware of the findings and develops an anxiety reaction to them. Such gross incongruities between the severity of the symptoms and the structural changes are immediately striking to the experienced physician.

Residual psychogenic rheumatism, in our experience, most frequently follows trauma to the musculoskeletal system; less often does joint disability persist after subsidence of a primary rheumatic disease such as rheumatoid arthritis, rheumatic fever, gout, etc. After some minor injury, the symptoms of which ordinarily would subside in a few days or at most a few weeks, these patients may have intractable symptoms for months or even years. Among soldiers persistent disability following minor back injuries was particularly common; often recovery failed to result even after prolonged rest in bed or immobilization. In such cases a gradual change in the nature of the symptoms usually develops as time goes on. Although the initial symptoms may be typical of organic disease, the complaints eventually assume obvious functional characteristics and associated psychoneurotic manifestations in other systems may appear.

Functional Characteristics of Presenting Disability.—The most common symptoms are " pain ", tenseness, stiffness, limitation of motion, subjective sense of swelling, muscular fatigue, and weakness of an involved part. The complaints more often are generalized, are " all over ", but may predominate in one region or another. Sometimes they are vague in quality and location—" Can't quite tell you where it is or what it's like ". Mental distraction at a movie, football game, or social gathering may give temporary relief, and exacerbations with or following episodes of emotional stress or mental fatigue are almost the rule. Pain is practically a universal complaint, but on close questioning often has functional characteristics. It may be fleeting or constant, " bad all the time ", " present day and night ". Salicylates often have no effect, and local heat and other physiotherapeutic measures fail to give relief or " make things worse ". The distribution of pain often is not anatomical; instead of being located in or about joints, for example, it may skip " here, there and elsewhere " with utter disrespect for anatomy. Such sensations as weakness, fatigue, pricking, tingling, numbness, deadness, burning, fullness, and pressure may be interpreted by the patient as pain. On analysis the victim

may not have pain at all in the strict sense, but only paraesthesia. When aching and stiffness are the predominant symptoms, usually they fail to fluctuate with external environmental factors such as weather changes, physical activity, etc. The discomfort in patients with psychogenic rheumatism almost invariably is augmented by use of the involved part.

On physical examination varying degrees of muscle spasm may be found, and, when marked, may be accompanied by limitation of joint motion. A tense, anxious, defensive, or antagonistic attitude is often apparent. On examination the patient may be fearful or resistant, may cry out with pain on palpation or movement of a joint which is apparently normal, may over-react, jump, grimace, or groan on light palpation of the erector spinae muscles, or may grasp the examining hand in protest against being hurt: in general, there is a " touch-me-not " reaction. In soldiers, as in compensation cases, major hysterical conversions as manifested by bizarre limps, gaits, and postures are displayed occasionally (see illustrations, pp. 214–215).

Positive Diagnosis of Psychopathology.—To establish positive evidence for the diagnosis of neurosis is just as important as ruling out organic disease. The functional nature of the presenting complaints, as already discussed, the presence of other psychoneurotic symptoms, the patient's past history and family history of emotional instability, and the presence of an exciting mental conflict, allow this to be accomplished.

Evidence of Coexisting Psychoneurosis.—Associated functional manifestations (headaches, dyspepsia, globus hystericus, sighing respirations, praecordial pains, insomnia, tremors, cold moist hands and feet, anxiety, nervousness, etc.) are present in the majority of cases. Such psychoneurotic complaints were present in forty-six of fifty (92·0%) soldiers with psychogenic rheumatism studied at Hoff General Hospital, and in 179 (89·5%) of 200 cases studied at the Rheumatism Centre, Army and Navy General Hospital. An interesting test was made by Flind and Barber (1945), who submitted seventeen patients with psychogenic rheumatism to a swimming test; all but one had to give up " after a few yards " because " it was too frightening ". Weiss (unpublished) attempted to make precise psychiatric diagnoses in forty patients with functional musculoskeletal disabilities; hysteria was diagnosed in sixteen patients, anxiety states in eleven, hypochondriasis in two, psychotic depressions in two, an " underlying neurotic character " without specific classifications in nine.

Psychoneurotic Predisposition.—In practically all instances evidence of previous neurotic traits may be elicited. Such traits present in childhood and persisting to adult life suggest a liability to neurotic reaction under stress. Past histories of enuresis, somnambulism, nightmares, temper tantrums, morbid fears (fear of darkness, of death, or of illness), stammering, fainting spells, etc., are given by many. Boland and Corr (1943) found that approximately one-third of their cases had experienced disabling psychoneurotic or hysterical episodes before the onset of psychogenic rheumatism. These ranged from attempted suicide to interruptions in schooling because of " nervousness ".

Halliday (1943) believes that most patients with psychogenic musculoskeletal

disabilities have similar personalities. He pictures them as displaying obsessional trends with self-limitation and restriction of feeling. As children they are said to be shy and in later life are over orderly, punctual, and clean, tending to live quietly—often as " home birds ". He contrasts this personality with that found in patients with functional dyspepsia or peptic ulcer, described as showing compulsive drives, over-emphasized activity, efficiency, and independence; being especially susceptible to threats against security and to changes of authority. However, various types of personalities have been found in our patients. Not all of them have been " mousy fellows "; some have been dynamic extroverts and others frank exhibitionists, especially those displaying gross hysteria.

Precipitating Emotional Factors.—These are often difficult to ferret out as the patient may be unaware of them himself. Multiple interviews are frequently necessary to elicit the environmental factors or external events which precipitated a deep-seated emotional reaction. Only by following the sequence of happenings before the onset of symptoms can clues be found in some instances; then, once the clue is found, pressing direct questions will often cause the patient to expose the disturbing event or circumstance.

The precipitating factors which cause frustration in civil life are manifold; most of them provoke a sense of grief, rage, or guilt. Hench (in publication) cites a few examples: " a stern parent interfering with a child's social development; an unattractive girl dominated by her protective mother and afraid the boys were passing her by; a person who previously was ' impressed ' by her parents and who considered herself ' impressed ' by her in-laws; a veteran forced by the housing shortage to live with in-laws (enough to give anyone psychoneurosis!); a common American trouble—' one vacation in ten years '; sexual impotence of the patient or the marital partner; June–December marriages; a spinster who had given up marriage to care for her mother, whom she had thereafter unconsciously come to hate; fear of an unfaithful, drunken husband; a patient whose relative died of ' rheumatism ' and who feared that his own rheumatism might also be fatal ".

Among military personnel additional factors existed to induce anxiety. These included: (1) the loss of security or love caused by separation from a wife, family, or home; (2) the loss of ability to control one's personal destiny; (3) resentment at authority, especially when such is invested in those felt to be inferior; (4) fear of bodily harm; (5) confusion resulting from strange surroundings, crowding, regimentation, and competition; (6) the concern for the safety and financial well-being of dependents; (7) indignation over lack of promotion; and (8) worry over fidelity of wife or fiancée.

Psychopathology.—Weiss regards " smoldering resentment " to be the common basic psychopathology in psychogenic rheumatism. He pictures resentment as breeding chronic discontent and a feeling of rebellion. But the outward display of rebellion is inhibited for one reason or another, such as filial respect or fear of authority. The continuous sense of hostility, according to his concept, prevents the patient from relaxing, with the result that constant muscle tension develops which leads to symptoms of aching, tenseness, and muscular fatigue. Regardless of the underlying psychologic mechanism, the somatic effect of chronic muscle spasm appears plausible. This can be appreciated by most physicians who have experienced muscular aching and fatigue after periods of prolonged nervous tension.

Localization of Symptoms

It is interesting to speculate why the psychoneurotic individual may subconsciously choose the musculoskeletal system for expression of somatic symptoms. In most instances fixation is probably prompted by past or present experiences, or by expediency. In cases of superimposed and residual psychogenic rheumatism a present or immediately preceding example of a type of disability is suggested to the patient. In cases of pure psychogenic rheumatism such examples, though not as direct, may be found also. In one-third of our patients (Boland and Corr, 1943) examples of arthritic invalidism were present in the immediate families; and approximately two-thirds gave a history, recent or remote, of traumatic or inflammatory joint disease in their past lives. Had examples of stomach trouble existed instead, it is probable that some form of functional dyspepsia rather than psychogenic rheumatism would have developed in response to the same emotional stresses.

The back and lower extremities were the favoured sites for localization of the predominant complaints in soldiers. Boland and Corr found that in thirty-eight of fifty soldiers (76%) the predominant symptoms were located in these regions. They suggested that this election of somatic fixation bore an expedient relationship to the attempted solution of an emotional conflict, " as these structures are synonymous with marching and soldiering ".

Differential Diagnosis

Primary fibrositis is the principal rheumatic condition from which psychogenic rheumatism must be distinguished. In both conditions the diagnosis is based largely on the qualitative characteristics of subjective complaints, and differentiation may require a detailed analysis of the symptoms. Hench and Boland (1946) have listed the chief points which allow these two syndromes to be differentiated. The accompanying table is adopted from their summary.

Terminology

The term psychogenic rheumatism has not suited all rheumatologists and psychiatrists. Some (Weiss, unpublished) contend that the word rheumatism is too vague and already is surrounded by enough opprobrium without linking the word psychogenic to it. But functional muscle and joint complaints are often vague too, and the word psychogenic at least points to the origin of the symptoms. The word psychosomatic is objectionable because more and more it is being used to imply that actual organic changes are caused directly by mental influences. Whereas, this may be true in certain structures, evidence does not support those who suggest that certain common organic joint diseases may represent psychosomatic disorders. Psychiatrists prefer to use psychiatric diagnoses based on underlying psychologic processes to catalogue the musculoskeletal symptoms, using such terms as anxiety-depressive state, conversion hysteria, hypochondriasis, etc. However, internists and orthopaedists cannot be expected to be trained psychiatrists, any more than psychiatrists can be expected to be trained rheumatologists. In practice the diagnosis of functional disease starts by recognizing that the complaints and findings do not conform with those found in organic disease. The first tip-off is the qualitative characteristics of the bodily symptoms; exploration of psychologic deviations come later. Designations such as " psychoneurosis ", " anxiety state, as manifested by musculoskeletal symptoms ", etc., may be more accurate but are cumbersome. Although objectionable to some, the term " psychogenic rheumatism " is

convenient and compact; if its limitations are understood it can serve as a useful label, at least until a better one comes along. It matters little if some object to the name as long as they accept the fact that not all aches and pains in and about muscles and joints are due to organic disease of these structures.

DIFFERENTIATING POINTS BETWEEN PSYCHOGENIC RHEUMATISM AND PRIMARY FIBROSITIS

TABLE

	Psychogenic Rheumatism	Primary Fibrositis
Patient's attitude	Tense, apprehensive, " subjective ", often antagonistic or defensive.	Usually " objective " and co-operative.
Chief symptoms	Often vague. On analysis " pain " may consist of such sensations as burning, tightness, fullness, numbness, weakness, tingling pressure, or " queer feeling ". Muscles and joints may be " tense " rather than stiff.	Usually definite. Consist of aching, soreness and stiffness.
Factors influencing symptoms	Symptoms, in general, fluctuate with changes in internal or mental environment: tend to be worse during or following emotional stress, and temporarily relieved by mental distraction (theatre, social gathering, football game, etc.).	Symptoms fluctuate with changes in external or physical environment: made worse by physical inactivity and damp weather, and ameliorated by dry warm weather, physical activity, local heat, etc.
Degree of disability	Variable but may be severe and always disproportionate to physical findings. Disability may be greater than with serious joint disease.	Usually not marked—symptoms are a " nuisance " to patient.
Constancy of complaints	Tend to be constant, " bad all the time " or " getting worse ". Exercise almost always aggravated.	Subject to exacerbations and remissions; may last days or weeks, then disappear. Intensity varies during day; worse in morning and after physical inactivity, better after mild exercise.
Location of symptoms	Often not anatomical, may " skip here, there, and everywhere ".	Anatomical. If symptoms migrate they do so with respect for anatomy of joints and muscles.
Response to examination	Patient often over-reacts, is tense, and resistant; a general " touch-me-not " attitude.	Co-operative. Pain and tenderness are consistent, and mental distraction is without effect.
Response to treatment	Variable, but often nothing relieves. Salicylates frequently are ineffective and local heat may make worse; alcoholic beverages relieve temporarily.	Temporary relief from salicylates, local heat, and other physiotherapy.
Associated functional complaints	Almost invariably present, i.e., nervousness, tremulousness, cold, moist hands, insomnia, globus hystericus, headaches, sighing respirations, bizarre postures and limps, etc.	Usual minimal or absent.
Positive evidence of psychopathology	Present, i.e., psychoneurotic predisposition, precipitating emotional conflict, underlying resentment or frustration, coexisting anxiety, depressive, hypochondriacal or hysterical reaction, etc.	Usually absent.

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(*For Illustrations to this Article see pages 214 and 215*)

PSYCHOGENIC ARTHRALGIA*

BY

HENRY P. WRIGHT

Montreal

Today the term " psychosomatic syndrome " needs no introduction or explanation to the average intelligent physician. It is generally accepted that disease symptoms may be aggravated by emotional disturbance producing pathological changes through the sympathetic or endocrine system, as, for example, in coronary sclerosis. Also, most experienced rheumatologists emphasize the important contributing effect of emotional disturbance in rheumatoid arthritis. This paper, however, is confined to cases in which no organic disease of the joints has been detected. Therefore the term psychogenic arthralgia is suggested, rather than the older one of psychogenic rheumatism.

Psychosomatically speaking, such conditions as headache, laughter, tears, flushing, vomiting, heartache (or, if you like, coronary spasm) are frequently manifestations of disturbed psyche—and so it is with changes in the joints. Forty-five years ago my own younger brother avoided church-going on more than one Sunday with a painful knee, which always seemed to clear up while the rest of the family were at church. Early in the world war 1914–18 the classification of the psychoneuroses was confused, and the term " shell shock " was at first generally applied to cover bizarre and unfamiliar clinical entities. But gradually the so-called functional cases were divided into three groups: (1) hysteria; (2) neurasthenia; (3) malingerers. In the interval between the two world wars, psychiatry became a respectable medical speciality, perhaps partly due to the increasing number of cases in this group and the decreasing number of the more serious epidemiological diseases such as smallpox, typhoid fever, etc. Add to this, in our civilization, the transition from the horse-and-buggy stage to the era of large cities, telephones, automobiles, aeroplanes, and preventive medicine, and the above idea becomes at least suggestive.

The power of emotion in the direction of human thought, the impotence of logic to affect the conclusions dictated by passion, prejudice, and fear, and the extent to which man's mind is controlled by psychological processes of which he is himself entirely unconscious, have been so abundantly demonstrated as to become obvious to the most superficial observer. Rationalization allows the mind to regard incompatible facts in such a light that their incompatibility is more or less efficiently cloaked. The man whose commercial morality differs fundamentally from the code which he practises in his private life persuades himself that the latter code is not properly applicable to business relations—that a man must live and the apparent immorality involved disappears when it is necessary

* Read before the Annual Meeting of the Canadian Rheumatism Association on May 12, 1947, at Sunnybrook Hospital, Toronto, Ontario.

for the support of one's wife and family. The extension of this principle in time of war when conflict continuously exists between the self-preservation instinct and the herd or moral one, often called discipline, esprit de corps or " morale ", make an understanding of the subject under discussion at least comprehensible to the most pathologically-conditioned physician. To the young physician of today, psychology is as familiar as the Bible was to his Victorian confrère.

Hench and Boland (1946) have stated that in war time over 16 per cent. of cases in the Army Rheumatism Centres were primarily psychogenic. Halliday (1937), Boland and Corr (1943), and Edmonds (1947) have also made important contributions to this subject. No figures are yet available for civilian life, but it is my belief that when the medical profession is alert and on the look-out for this sort of case, the diagnosis will be made with considerable frequency and yield more surprising results than those obtained by physicians who are familiar with and on the alert to diagnose that frequently missed arthritide, which has been known for so many years under the name of *gout*.

Case Reports

The following cases will illustrate the two fundamental types most commonly encountered in practice. Both patients were civilians, with whom, presumably, most physicians will be primarily concerned.

Case 1

A young woman, 34 years of age, had lived at home in Montreal and worked in a well-known industrial concern for many years, with satisfaction to her employers and herself. About one year previous to consulting me, she married and moved to Halifax. She was referred by a dentist, to whom she had gone to have her teeth extracted because of pain across the shoulders and in both hips, both legs, and both hands. She stated that she thought the dampness in Halifax was the cause of her trouble, which had been present for the last seven months. There was no history of trauma, fever, or chills. The initial joint involved was the right arm, and from there the pain had spread to her back, shoulders, and legs. The pain was severe, but there was no swelling, redness, or heat. She did not know what time of day the pain was most acute, and it did not keep her awake at night. The present function of the joints was unimpaired, and since she had returned to Montreal she was slightly improved. She thought she had lost 3 lb. in weight.

The family history revealed that the mother had arthritis and her only brother was said to suffer from an ulcer of the stomach. Also the mother and brother both had ragweed hay-fever. The patient said that the present complaints began ten days after her marriage, when she was living in Halifax in an apartment, doing her own work and seeing relatively few friends. She thought she was somewhat nervous, but her appetite was good and she ate a well-balanced diet. For recreation she indulged in walking, going to the movies, and playing bridge. She drank four cups of coffee and two cups of tea daily, smoked about twenty cigarettes a day, and had an occasional cocktail. While in Halifax she had consulted a physician for the complaints above-mentioned, and he had given her injections of vitamin B, but without effect. Radiographs had revealed nothing, and the sedimentation rate was normal. Her menstrual history was, as she stated, apparently normal.

Physical examination revealed a normal-appearing young woman, 5 ft. 3½ in. tall, and weighing 133 lb. There was slight nystagmus in the left eye. The pulse rate was 80 and was regular and of good volume with compressible vessel walls. Blood pressure was 140/80 mm. Hg. The heart, lungs, abdomen, and central nervous system were apparently normal. The skin was dry and clear, the muscles well-developed, the hands cold. There was some slight tenderness in the joints in

which she complained of pain, but otherwise, both objectively and functionally, they were normal. Haemoglobin was 85 per cent., red cell count 4,720,000 per c.mm., white cell count 8,800, and sedimentation rate 6 mm. in the first hour. (Radiographs were not made because of the past history of negative findings in Halifax.)

Gynaecological examination revealed an imperforate hymen. She was, therefore, referred to a gynaecologist and his report was: " Patient had had an intact hymen which had been unbroken after six months of marriage. Dilatation of the hymen revealed an unhealthy-appearing polyp hanging from the cervix. The uterus itself was normal in size and the pelvis was good. The adnexa was negative. Under pentothal the hymen was further stretched, and there was a stricture at its base which required plastic treatment to the introitus; in performing this the opening was further enlarged. The cervix was dilated up. The polyp, whose base lay somewhere in the region of the internal os, was removed. Further dilatation of the cervix and curettage of the uterus itself revealed no abnormalities. A sulphathiazole gauze pack was inserted."

She returned home, and some weeks later enthusiastically grateful letters were received both from the patient and her husband.

This case was presumably one of psychogenic arthralgia caused by dyspareunia and failure, through modesty, to consult a gynaecologist because of her difficulties. It emphasizes the necessity for careful routine examination of all systems by the rheumatologist, when the case is not absolutely straightforward. In the old days a consultant was supposed always to look at the eye grounds and make a rectal examination: I would add to that today, in the case of females, vaginal inspection and examination, or examination via the rectum. It is perfectly obvious that in such a case as the above psychiatric advice is not indicated or required.

Case 2

The second case is that of a patient whom I have not personally seen; but as a result of an article published three years ago on the recognition and treatment of gout the following letter was received:

> " In *Modern Medicine* I read a short article by you on ' Recognition and Treatment of Gout ', and find that undoubtedly I have something like it—or have gout. For fifteen years I have had wicked headaches and an ' all body aching ', that nothing stopped. My husband, an M.D., use to try all the various remedies to help me, and finding nothing that ever stopped them gave me up more or less as a neurotic—although heaven knows anyone could tell by looking at me that I could hardly put on that devastating illness. After twenty-four to thirty-six hours' of misery I'd get well, only to be laid low in a few days with another.
>
> In September last, after an absence from home for some time, my four grown children and I were to be together again. I dashed home, only to find the grass had grown, tried to mow the grass to make the place look better, furiously cleaned house, had a good chicken dinner ready for my family—only to come down so sick with swollen feet and hands and the most awful pains in my feet, pelvis, and head. Oh, I was really ill. My son, a young M.D. in the Army, laughing said ' Mother, dear, you have a mean case of gout '. All thought it was a huge joke and told me to give up my ' likker ' (I don't drink), etc. For a week I was too miserable to care, although I was heartbroken on being the cause of such a miserable time for all. However, my son did tell me to leave everything to eat alone except milk and bread until I was better. It took me six weeks to get my shoes on and ever since I have a miserable time if I eat anything except bread and milk!
>
> I have always had a fine appetite and digestion. Have done all my work, raised four children, helped my husband in his medical practice by running errands, etc., taken care of the yard, and been a healthy mortal, and now I'm reduced to bread and milk and aches and pains. Is there any cure? I can't take cinchophen. At least when I have, I have had face and hands swell up very badly and feel horrible. I am just now getting on my feet again after eating about a teaspoonful of chicken salad five days ago. Either I have a vivid imagination or it's fact, but I think nearly everything I eat fills me with misery. Coffee, tea, cocoa, and apricots put me on the sick list for ten days a while ago. My feet

are quite deformed and are losing surface feeling. I suppose I'm a ' gone grey goose ' —but I'm writing to see if you have any other suggestions to follow. I noticed that in your acute stage diet you list eggs. I'm going to eat one as soon as I get a little better and see what it does to me.

At present I'm helping to care for an aged mother and two-year-old grandson, whose father was a war casualty, but if you'd like to use me as a guinea-pig, I'll try things out and report to you. This thing is really a horrible thing to have and if anything can be done to help someone else through me it would be worth while. My family is grown up and gone; my husband in love with his secretary, so I am more or less free.

Listed as premonitory signs you have dyspepsia. In my case it is a wild craving for good things to eat, salted nuts, olives, anchovy paste, and fried chicken, snappy cheese, rare beef roast, chops and steaks, of which we don't have so much recently—raisins, etc., and if I don't watch out I'm sick. Under your ' at no time ' list of food I have never eaten kidney or brains, but everything else has generally been on our menus. Asparagus and lima beans have made me ache too. My son said he didn't have time from his Army duty to watch my case, but so few women had gout that perhaps I had something else. I can tell when I'm going to be sick, first by remembering the good things I've eaten then by swollen hands and feet and being easily upset by people, and the aching in my hips and twingy pains in my feet. I am getting worse I know, because I can hardly go up two steps at times. In am 53 years old, 5 ft. 8½ in. and weight 149 lb. Three years ago had all of my teeth out to ' cure ' the rheumatism in my feet!! Rarely have colds, the last one fifteen months ago. Have never had the children's diseases when a child, or when my children had them. Had malaria in 1910, appendicitis acute in 1912, Todd-Gilliam in 1923 or 4, after I had had several miscarriages due to retroversion. My children are healthy and strong, although I'm afraid one daughter living in California and 23 years old may unfortunately have inherited this thing. Recently she has written me of having the ' same sort of headaches you used to have ' and added that she wasn't ever going to eat chocolate again as she was sure that caused it. The two grandchildren, the boy, 2, I'm caring for, has a cow's milk allergy, and the little girl in California, 1 year old, is healthy.

My father, an M.D., died 12 years ago of coronary occlusion. My mother 86 years old is spry, wiry little lady who fractured her back in a fall last May and was walking in August. She is very well and eats everything. Three brothers and one sister are healthy and well too.

Please don't feel that you must answer this letter. I suppose there's no cure, but I felt I'd like to ask you, anyhow. You stress early recognition that in my case was not done, but it would be early recognition for my daughter. Do you think I have gout or is it some form of arthritis? "

In my opinion, this case is obviously one for a psychiatrist, after investigation by an internist or a rheumatologist, and a rheumatologist should always have the point of view of an internist. Medicine seems to be changing its pattern, and during this period co-operation is more than every necessary, because with the enlarging field it is impossible for the general practitioner to survive in the same position as he occupied during the Victorian era. How much co-operation is necessary in this second case would depend on the physical examination and laboratory tests, but it is conceivable that more than one physician would be required to solve the patient's difficulties.

Summary

The importance of psychogenic arthralgia is emphasized and two cases reported of widely different character, obviously requiring different forms of therapy.

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A CASE OF CALCINOSIS CIRCUMSCRIPTA

BY

DOUGLAS L. WOOLF

Calcinosis, or chalk gout as it is commonly named owing to the tophus-like swellings it presents, is a slowly progressing condition of unknown aetiology and pathogenesis. Two types are described, circumscripta and universalis. The female sex is the more commonly affected. The circumscripta variety usually occurs in those in middle or late life.

Discussion

Atkinson and Parkes Weber (1938) from whose paper most of the references given below are quoted, state, in a complete survey of the condition, that the first case of calcinosis was described in 1878 by H. Weber, and that Leissier in 1877 recorded the case of a woman aged 21 years who had had since childhood hard nodules in the skin and subcutaneous tissues: there was a discharge of chalky particles, and he believed his case to be one of gout associated with scleroderma. In 1844 Virchow described metastatic calcification in nephritis. In 1899 Derville published a case, and in the same year Durett suggested a familial incidence, but this was not proved. In 1900 Profichet wrote a thesis on calcinosis, with a résumé of all cases published up to date. It was afterwards called by foreign writers the syndrome of Profichet. Riche reported a sulphuric-acid worker who formed nodules of calcium carbonate and phosphate. In 1902 Hutchinson reported a case of a woman aged 58 years who probably suffered from scleroderma; the fingers felt wooden, and calcareous plaques were found in the deep layers of the skin of the forearms. This seemed to be a case of scleroderma with calcinosis, and was the first published in England.

Lehrenbecker in 1927 described a patient who had formerly undergone bilateral sympathectomy for Raynaud's disease and in whom calcification later supervened. The author wondered whether the operation had been the exciting cause of the calcinosis.

Steinitz (1930) reported a case in a woman aged 82, the oldest patient on record. Brauer believed ovarian function was diminished and that this fact had something to do with calcinosis. He also believed that circulatory disturbances might have favoured a chalky deposition. Wilson (1935) thought the deposits of calcium phosphate found in the fingers of one of his cases might have been due to an endogenous hypervitaminosis D connected with an unusually high blood cholesterol, superimposed on old Raynaud's disease which had remitted. The same authors state that sclerodactylia and scleroderma are frequently associated, the joints remaining free. They state that calcinosis universalis may be fatal.

Comroe (1944) states that the circumscripta variety is usually restricted in

distribution to the articular region of the phalanges and the extensor aspects of the knees and elbows. Calcium metabolism reveals no abnormality, and no demineralization of bone or arthritic changes are seen.

Pedersen (1943) says that the French call the condition "concretions calcaries des atrophies cutanées". He describes a woman at the menopause who had typical calcinosis circumscripta with a tendency to blue and cold hands. He excludes correlation between calcinosis and changes in the endocrine system, as in three cases post-mortem changes showed no abnormality in the latter system. He also thinks that the marked correlation between calcinosis and acrocyanotic conditions and scleroderma suggests some abnormality in the blood stream.

Pedersen (1943) gives the chemical composition of calcium deposits from a patient with calcinosis. There were moist brown tough lumps with a hard central core. The tough part was muscle fibre, the remainder, stony core. Analysis showed the presence of calcium, phosphate, a little carbonate, and a faint trace of magnesium, but no oxalate or uric acid. He concludes that the core was very similar to bone. Wigley and Hunter (1945) describe a case of calcinosis in chronic nephritis with secondary hyperparathyroidism. The patient died, and necropsy revealed chronic nephritis with shrinkage of the kidneys. There was hyperplasia of all four parathyroid bodies.

Of treatment, Comroe (1944) states that hemithyroidectomy and parathyroidectomy have been tried with little result. Pedersen (1943) states that one case responded to rest, colchicum, cinchophen, and mud packs. Atkinson and Weber (1938) state that drugs, physiotherapy, dietetic, and glandular and surgical treatment have been tried with no certain success. Hunter experimented with fibrolysin, Hoffman with hydrochloric acid, Weissenbach used thiosinamine, iodide, and thyroid gland. Chopra gave sodium phosphate for long periods, finding that the formation of nodules was thus prevented. Thyroid and ovarian extract were of no benefit when tried by Weil, Weissmann-Netter, and Brauer, though Werley claimed improvement from thyroid extract. Chopra found that anterior pituitary gland with small doses of thyroid reduced the size of the nodules. The use of *x* rays removed the nodes in a case described by Borak. Drucker thought radium useless, but Ducasse found that the nodules became liquefied with this treatment. Ramsdel performed unilateral thyroidectomy in one case. The parathyroids appeared normal, and great improvement followed; 50% of the nodules disappeared, and the crippled girl became active and resumed her duties. Brody and Bellin considered that the benefit of parathyroidectomy lay in its causing less saturation of the blood-serum with calcium, and in a tendency for the deposits to be decreased. Sheldon at the Royal Society of Medicine on March 25, 1938 (Atkinson and Weber, 1938), showed a child from whom the calcareous deposits had disappeared without any special treatment since the case was originally demonstrated in 1936.

The following case is reported owing to the widespread calcinosis and its response to local surgical treatment.

Case History

A man aged 40 years was first seen at the British Red Cross Rheumatism Clinic in December, 1942. He gave a history of the presence of small hard swellings for the past twenty to twenty-five years, the first one being on the left shin; both knees and elbows next became affected, and more recently firm nodules had developed on the left hand. If injured, the nodules became painful, whilst at other times they were inflamed and swollen. The patient's chief complaint was of the unsightly appearance of the nodules. There was a history of the nodules breaking down and discharging: they did not reappear at these sites.

He had no other symptoms, and there were no symptoms of circulatory disturbances. There was no family history of deposits. An elbow nodule had been excised, but a swelling recurred some three years after operation at the same site. His occupation had always been sedentary.

EXAMINATION.—Nothing abnormal was found in any system. There were multiple small nodules around the right elbow, and a larger firm area over the triceps muscle on the right arm and to a lesser extent over the left biceps muscle (Fig. 2, A). The noduies were marked over the left wrist and elbow. They were also present between the left tibia and fibula. Evidence of old ulceration and discharge was seen at this site. The patient showed no response to colchicum therapy.

INVESTIGATIONS.—At this stage the blood sedimentation rate (Westergren) was 7 mm. in the first hour, and 14 mm. in the second. Blood uric acid was 3 mg. per 100 c.cm. of blood; haemoglobin 89%; red blood cells 5,500,000 per c.mm. and white blood cells 7,100; the colour index 0·81%; and the blood calcium 10 mg. per 100 c.cm. A radiograph of the legs showed multiple disseminated calcinosis.

The patient's condition remained much the same until he reported again on July 4, 1946. He then complained of an increase in the size of the swellings, especially of the one over the posterior surface of the right arm. He also complained of limited movement of the right ankle joint.

Radiographs taken at this time of ankles, tibiae, elbows, wrists, and left hand, again showed multiple disseminated calcinosis (Figs. 2 and 3). There was an area of calcification over nearly the whole of the right triceps muscle (Fig. 2, B); subcutaneous deposits were also seen around both elbows and the left shoulder. Calcification involved nearly the whole of the left tibialis anticus muscle.

The sedimentation rate, blood uric acid, blood count, blood calcium and acid and alkaline phosphatase, and blood cholesterol were all within normal limits.

The patient was seen by the orthopaedic surgeon, and, in view of the unsightly appearance and discomfort caused by the large size of the triceps swelling, it was decided to explore and if possible remove the calcareous mass.

OPERATION NOTE (by Mr. W. D. Coltart).—The swelling was explored by an incision on the posterior surface of the arm. The posterior wall of the swelling was formed by the fascia of the arm, its anterior wall by the fascia on the posterior surface of the triceps muscle. On incision of the swelling about one pint of fluid with the consistency of white paint was evacuated.

The walls of the swelling were heavily encrusted with calcareous fragments, and it was possible to dissect away the whole of it, leaving the clean surface of the triceps muscle with its tendon below, although some difficulty was experienced in removing the whole swelling at its distal extremity, where it was apparently continuous with an olecranon bursa.

The wound was closed by suture of subcutaneous tissue, and the skin healed by first intention. The patient rapidly regained full range of movements and muscle power of the arm. (For post-operative radiograph see Fig. 2, C.)

HISTOLOGICAL EXAMINATION

The inner surface of the fibrous material contained calcareous material, and section showed a fibrous wall with haemorrhage on one side, and extensive deposits of calcium (Fig. 1). Inflammatory reactions were slight, as is usual with calcinosis.

A post-operative radiograph showed small residual areas of calcinosis. Further nodules are to be excised.

Summary

A case is described of calcinosis circumscripta in a man aged 40 years, with a history of twenty-five years' onset of nodules increasing in size; otherwise he was perfectly healthy. Laboratory investigations were normal. Radiographs showed multiple disseminated calcinosis. A mass over the posterior aspect of the right arm was removed and a layer of calcified fibrous tissue excised. A short survey is given of cases described in the literature and treatments used.

Conclusion

The case is of interest owing to the normal pathological findings and the inability to connect the condition with any circulatory disturbance or family history. The surgical treatment of the arm has so far proved satisfactory from a cosmetic point of view, and providing all the calcified material is removed there should be no recurrence.

I wish to thank the Medical Staff of the British Red Cross Clinic for permission to publish this case, and Mr. W. D. Coltart and Dr. Oswald Savage for their kind assistance with the preparation of this paper.

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FIG. 1.—Photograph to show the walls of the swelling heavily encrusted with calcareous fragments.

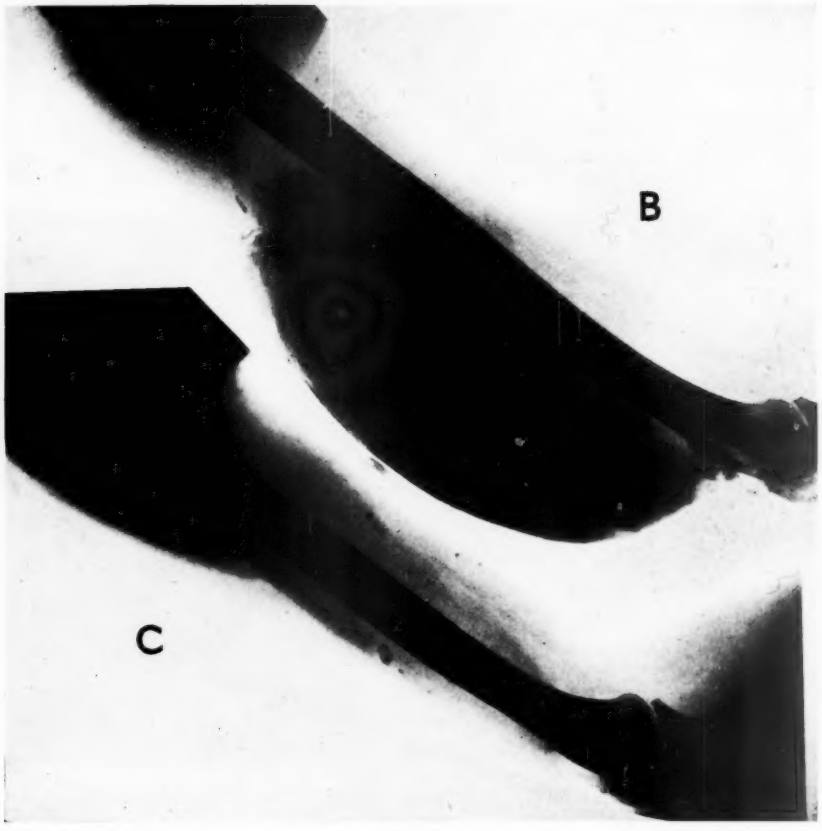


FIG. 2.—(A) Calcified mass on posterior aspect of right arm, left elbow, and wrist. (B) Radiograph of right arm before operation, showing calcified mass; and (C) postoperative radiograph.

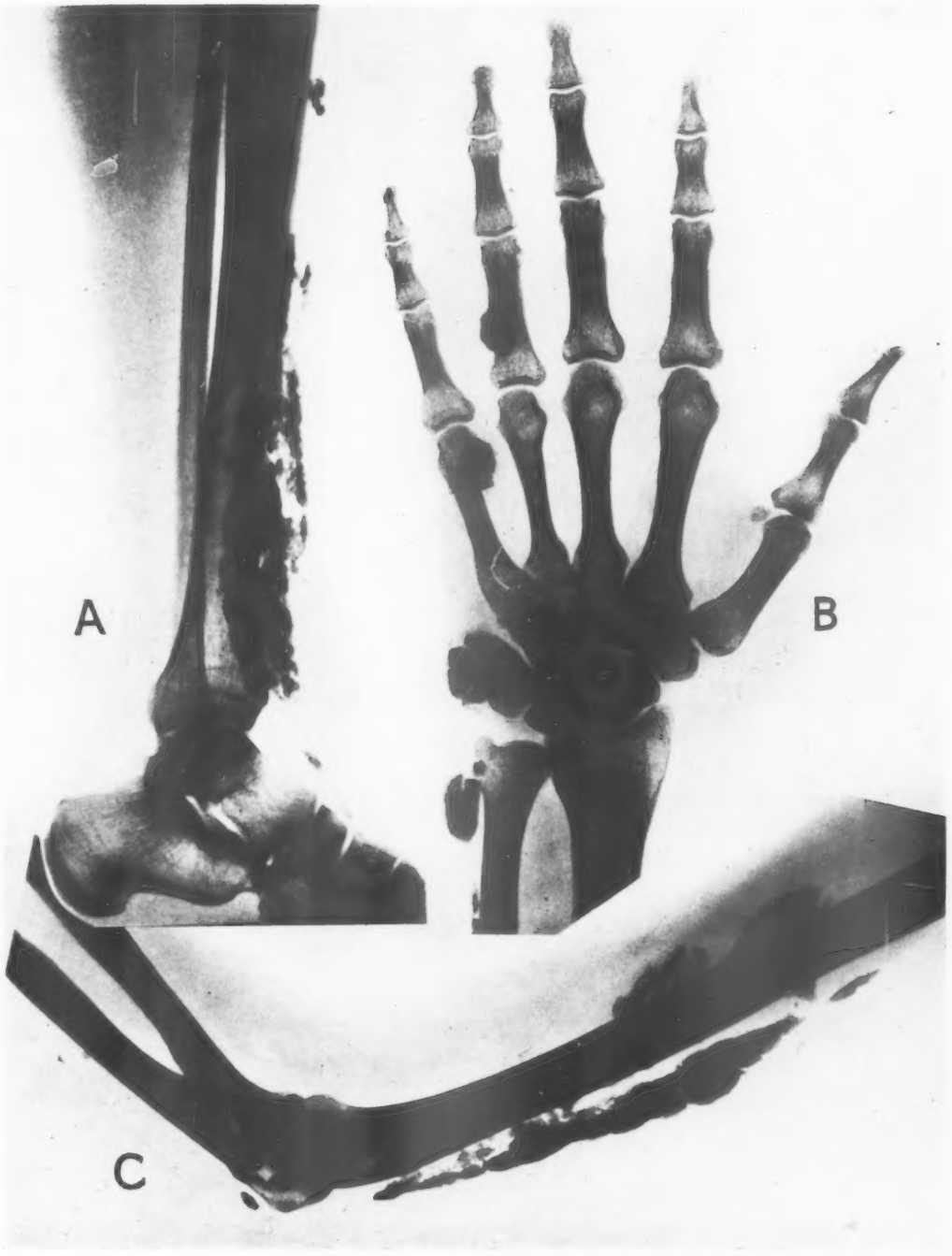
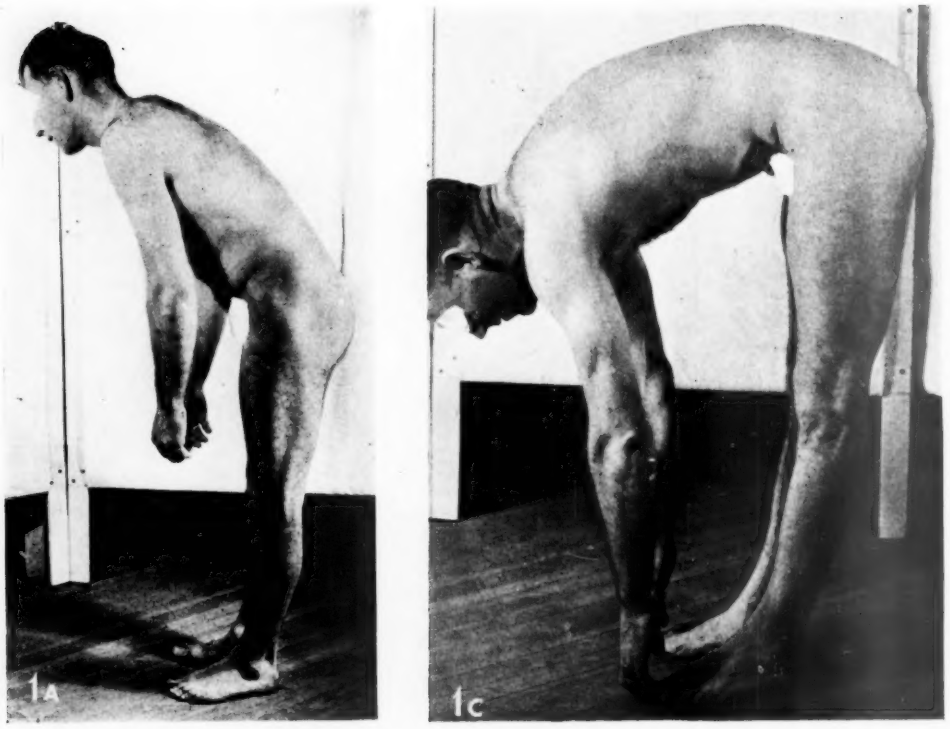


FIG. 3.—Radiographs of (A) left leg, showing extensive calcinosis; (B) left hand; and (C) left arm, showing calcified mass, but smaller than on the right arm.



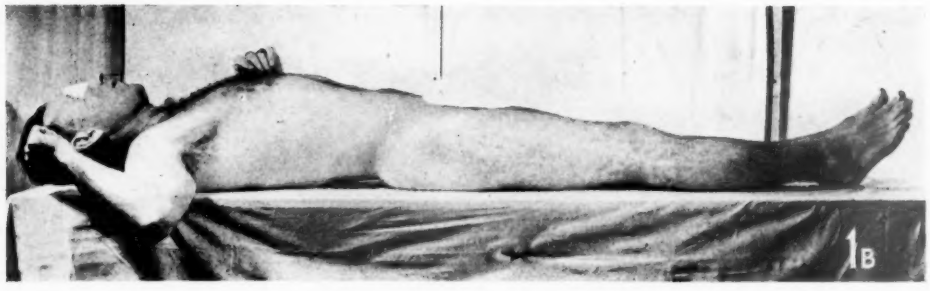


FIG. 1.—Illustrates hysterical bent back (camptocormia), the patient being unable (A) to straighten his back while in the standing position, although when recumbent (B) he can do so (note the lumbar lordosis), and although he can accomplish complete anterior flexion (C) without discomfort.

FIG. 2.—Another example of hysterical bent back. Postural correction resulted following narcosis studies and suggestion.

FIG. 3.—A hysterical bent knee. The patient could straighten the knee fully while lying but not while standing. He walked with a bizarre gait, throwing the foot outward and semi-squatting with each step.

FIG. 4.—Illustrating (A) hysterical deformity of the right hand of eleven months' duration. Under sodium amytal narcosis the patient was able to move the fingers normally. Radiographs (B) of the involved hand show marked diffuse secondary bone atrophy from disuse.

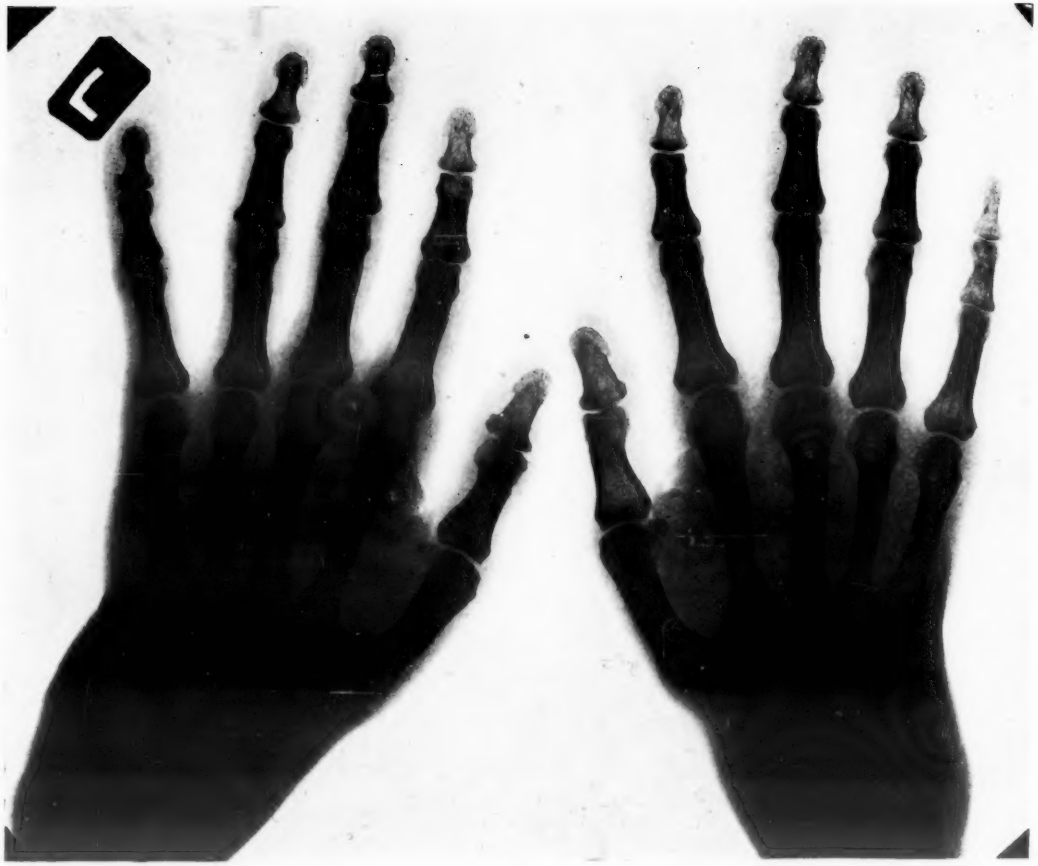


FIG. 1.

FIG. 1 (left).—Radiograph of hands showing punched-out areas in the first left interphalangeal and the second left metacarpo-phalangeal joints, originally diagnosed as being gouty in origin, but later shown to be subacute abscesses.

FIG. 2 (opposite page).—(*a*) Lymph gland, × 70, showing four necrotic germinal centres. (*b*) Lymph gland, × 375, showing detail of marked degenerative changes in one of these germinal centres, including small necrotic particles of pyknotic nuclear material, lymphocytes, histiocytes, and degenerated background.

FIG. 3 (opposite page).—(*a*) Metacarpo-phalangeal joint, × 4½, showing base of proximal phalanx. Note (A) proliferated synovial membrane directly covering a broad zone of normal bone. The articular cartilage is destroyed. (B) A subacute abscess. (*b*) Subacute abscess, × 600, showing polymorphonuclear leucocytes and lymphocytes.

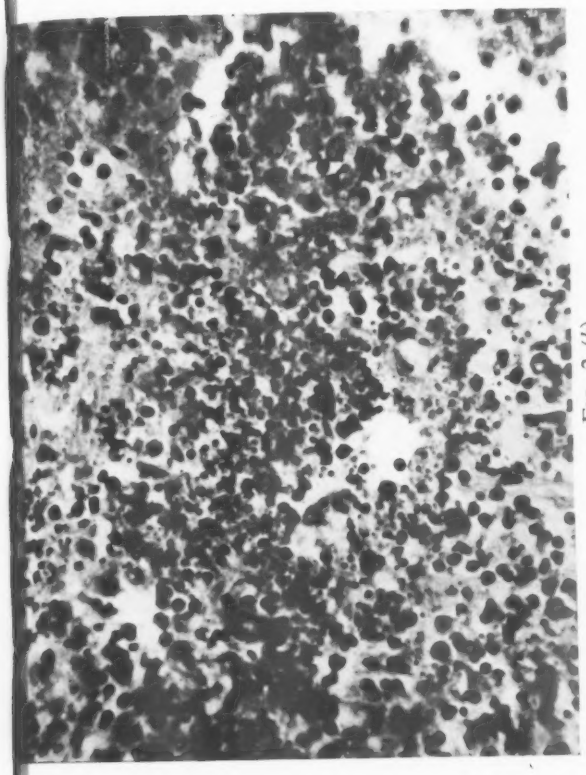


FIG. 2 (*b*)

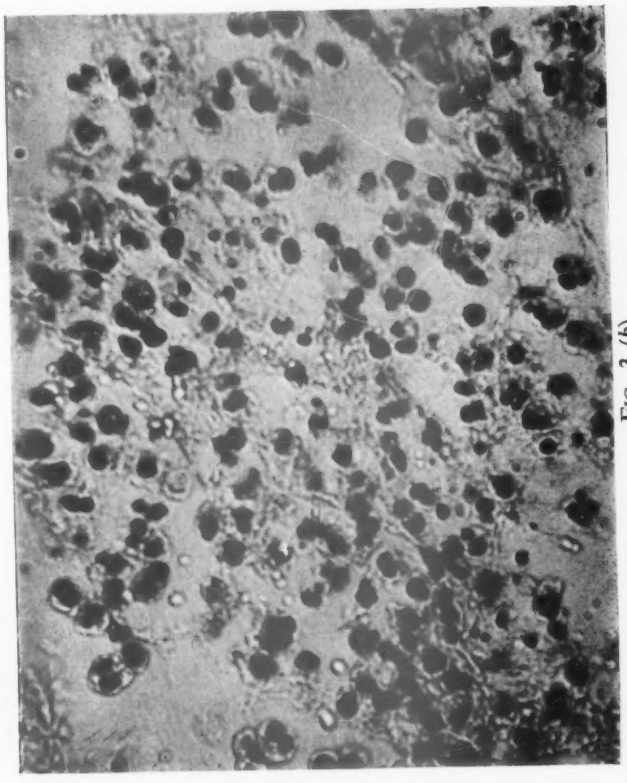


FIG. 3 (*b*)

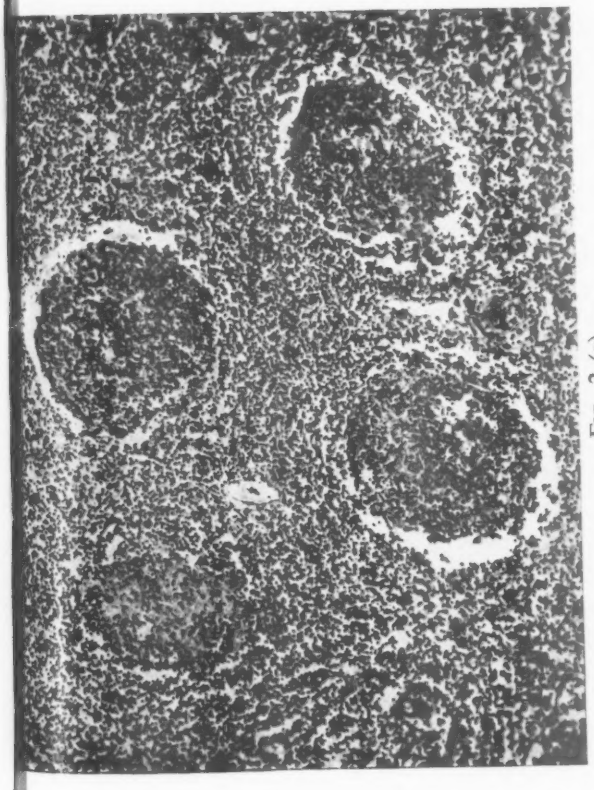


FIG. 2 (*a*)

FIG. 3 (*a*)

FIG. 1.—Subcutaneous nodules on the ulnar edge when arthritis was of 49 years' duration (terminal stage). Good general health.

FIG. 2.—Same case as Fig. 1. Subcutaneous nodule on right clavicle.

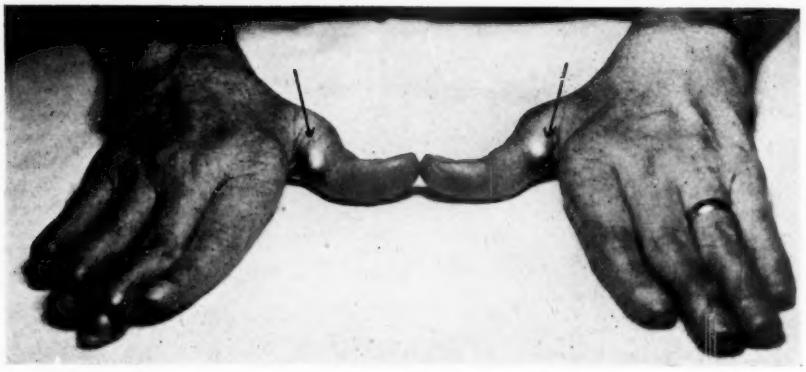


FIG. 3.—Subcutaneous nodules on the inner side of thumbs in a patient discharged as markedly improved by treatment. Rheumatoid arthritis of 8 years' duration (terminal stage).

FIG. 4.—Subcutaneous nodules (more than 10 years old) below the elbow joints. Rheumatoid arthritis at the terminal stage, of 15 years' duration. Good general health.

THE SIGNIFICANCE OF SUBCUTANEOUS NODULES IN RHEUMATOID ARTHRITIS*

BY

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The presence of subcutaneous nodules in rheumatic fever is of serious prognostic significance because, as they are pathologically similar to the Aschoff bodies found in the heart, they generally indicate severe cardiac damage and active infection. As a rule nodules appear after the onset of the rheumatic heart lesion. There is, therefore, practically always cardiac involvement in cases where nodules are found, and they may be regarded as presumptive evidence of carditis. Nodules develop occasionally, however, in cases in which no clinically demonstrable cardiac lesions exist. In 1889 Cheadle affirmed that the appearance of nodules was really the equivalent of a death sentence. While the prognosis is bad, it is not quite so serious as this suggests. Hayes and Gibson (1942), in a study of 167 patients with nodules, found that 163 had cardiac lesions. Fifty-two (31%) died during the attack, and the later mortality was double that of cases without nodules.

The Present Investigation

In contrast with this knowledge of the importance of subcutaneous nodules in acute rheumatism, little is known of the significance of their development in rheumatoid arthritis. We have, therefore, studied 55 patients with rheumatoid arthritis who had subcutaneous nodules; 38 of these suffered from rheumatoid arthritis only, while the remaining 17 cases had rheumatoid spondylitis as well. These 55 cases were found among a series of 290 cases of rheumatoid arthritis. Thirty-eight patients were female and 17 male.

The 55 patients had amongst them a total of 289 nodules, with the following distribution :

Head		3 (1·1%)
Trunk		51 (17·6%)
Limbs	upper	204 (70·5%)
	lower	31 (10·7%)

* Abridged from a paper read at the Annual Meeting of the American Rheumatism Association, held in New York City on May 24 and 25, 1946, and before the First Inter-American Congress of Medicine, Rio de Janeiro, Sept. 7 to 15, 1946.

In order to interpret the true significance of the subcutaneous nodules in rheumatoid arthritis, our cases were considered from four different aspects: (1) the patient's heart; (2) his joint involvement; (3) therapeutic results; and (4) the clinical features of the nodules.

The Patient's Heart

In assessing the prognosis for rheumatoid arthritis patients with subcutaneous nodules we must take into consideration the condition of the heart in such patients, just as we should do in cases of rheumatic fever, where the duration of life is governed by the extent of the heart damage. For some years we have observed that clinical examination of the heart in patients suffering from rheumatoid arthritis, accompanied or not by subcutaneous nodules, reveals no functional or morphologic abnormality notwithstanding the long duration of the arthritis or of the nodules. In view of the constantly normal findings, and for the sake of research, we decided to amplify our examination by systematic electrocardiographic and radiographic records of each case, and thus to obtain as accurate data as possible about the cardiac condition of these patients. The complete examination was carried out in only 19 patients with subcutaneous nodules. Thirty-six were subjected to clinical examination only, owing to the fact that we lost contact with the others before we had a chance to submit them to electrocardiographic and radiological examination.

It is significant that none of our 55 patients with rheumatoid arthritis subcutaneous nodules showed clinical signs of heart disease as a direct, indirect, or remote consequence of the arthritis, although 36 had suffered from arthritis for more than four years. The long duration of the illness in 8 cases (respectively of 13, 14, 15, 16, 17, 23, 30, and 50 years) is suggestive.

Electrocardiographic Findings.—In studying the tracings we took as a basis the recommendations of the New York Heart Association adopted by the American Heart Association and the Cardiac Society of Great Britain and Ireland. The three standard leads and praecordial leads CF_1 and CF_5 were selected.

Rhythm.—In none of the cases did we observe disturbances of rhythm, except for sinus tachycardia in some.

P Waves and P–R Interval.—These were normal in all tracings.

QRS Complexes.—In 3 patients there was left axis deviation due to hypertension.

Thickenings and notchings considered abnormal were observed in only 1 patient, whose radiograph showed moderate left ventricular hypertrophy, and whose blood pressure was 150/100 mm. Hg.

In one case there was bundle branch block. This patient was 64 years old, and the clinical examination showed striking aortic and pulmonary second sounds (chiefly the former) and a blood pressure of 200/100 mm. Hg. A moderately enlarged left ventricle was also found, and confirmed by radiograph. This patient being aged and having no history of previous rheumatic fever, the bundle branch block was attributed to coronary arteriosclerosis.

T Wave.—We observed a T-wave abnormality in a patient 66 years old with hypertension; this consisted in a flattening of T_1 that measured less than 1 mm. (myocardial sclerosis).

Fifteen patients showed normal electrocardiograms.

RADIOGRAPHS OF THE CHEST.—Eleven patients showed no changes in the size of the heart. The remaining 8 showed left ventricular hypertrophy due to hypertension.

From the analysis of these findings we may infer that there is no specific cardiac lesion in rheumatoid arthritis, no matter in what stage the disease may be or how long its duration. As a matter of fact we made a clinical, electrocardiographic, and radiographic survey of 50 patients suffering from rheumatoid arthritis and 12 from rheumatoid spondylitis in different phases of the disease, the duration of which varied from a few months to 41 years. In 72% of the cases of rheumatoid arthritis the results were entirely normal, while the remaining 28% showed abnormalities which were attributed to hypertension or myocardial sclerosis. The findings were normal in all patients suffering from rheumatoid spondylitis.

We may affirm that involvement of the heart is not found in rheumatoid arthritis, whether or not the latter is accompanied by subcutaneous nodules. In fact we know that rheumatoid arthritis, even when occurring at a young age, does not damage the heart. This we verified in 2 patients whose disease began at four and nine years old respectively.

When a patient suffering from rheumatoid arthritis shows signs of a cardiac lesion, either it suggests that another disease is accompanying the arthritis, or else it is the result of previous rheumatic fever. This is so true that, whenever it is difficult to differentiate between rheumatoid arthritis and rheumatic fever, the absence of signs denoting involvement of the myocardium will be a factor suggesting rheumatoid arthritis.

PATIENTS' JOINT INVOLVEMENT

Excluding the hypothesis of heart involvement in the cases of rheumatoid arthritis exhibiting subcutaneous nodules, we analysed the articular findings in our cases in order to judge whether there might be a more intense or graver form of arthritis in these patients. They were observed with special regard to their walking capacity, the direct and immediate consequence of the joint involvement.

We think it necessary to draw special attention to 3 patients with arthritis of 23, 30, and 50 years' duration, the last of whom began suffering at the early age of four years. All these patients were in good health, with slight joint involvement which allowed them to get about quite well in spite of existent ankylosis.

THERAPEUTIC RESULTS

In analysing the results of treatment we divided our patients into two distinct groups, the first of which included 40 in the advanced (37 patients) or moderately advanced (3 patients) stages, and the second composed of 15 patients in the terminal stage. Among the patients of the first group, 19 received treatment—thus enabling us to analyse its results—and 21 were untreated.

Among those who received treatment, 6 were much improved (marked objective and subjective changes with a considerable drop in the erythrocyte sedimentation rate), 9 were moderately improved (objective and subjective changes, together with a drop in the erythrocyte sedimentation rate), 3 showed no improvement (no objective, subjective, or erythrocyte sedimentation rate modifications) and 1 became worse (intensification of symptoms and increase of erythrocyte sedimentation rate).

Six out of 15 patients in the terminal stage received treatment. One was markedly improved (with 8 years of arthritis), 3 were moderately improved (cases of 9, 11, and 50 years of arthritis), and 2 showed no improvement (cases of 7 and 15 years of arthritis). These were considered good therapeutic results in view of the stage of the arthritis.

Thus, twenty-five patients exhibiting subcutaneous nodules (19 in the advanced or moderately advanced stages, and 6 in the terminal stage) received treatment, and favourable results were obtained in 19 (15 in the advanced or moderately advanced stages and 4 in the terminal stage). Six patients showed unfavourable results (4 in the moderately advanced stage and 2 in the terminal stage).

In commenting on the therapeutic results of these cases we should like to point out that in rheumatoid arthritis the results of treatment are much more favourable the earlier it is administered. Nearly all our patients were unfavourable from the point of view of treatment, in view of the duration of the arthritis. Nevertheless, the treatment results were satisfactory and in no manner inferior to those which we achieved with patients suffering from rheumatoid arthritis without subcutaneous nodules.

Clinical Features of the Nodules

The clinical features of the nodules (the time of their appearance in relation to the duration of the arthritis and to the activity or stage of the arthritis, and their response to treatment) were as follows.

Time of Appearance.—The appearance of the nodules in one patient occurred 11 years after the beginning of the arthritis, that is, at its terminal stage and with a normal erythrocyte sedimentation rate (7 mm. fall at the end of the first hour—Westergren). This goes to prove that, in contradistinction to the findings in rheumatic fever, the appearance of subcutaneous nodules in rheumatoid arthritis does not indicate activity or exacerbation of the arthritis.

In another patient the nodules had existed 20 days before we were notified of their presence, by which time the erthrocyte sedimentation rate was 9 mm. at the end of the first hour, and the patient himself showed an increase in body weight of 14·5 kg. since the beginning of treatment 15 months previously, the result of which had been marked improvement. This patient was discharged in excellent general condition and with practically normal joints.

In another case nodules appeared in the forty-ninth year of the arthritis—and, therefore, at the terminal stage—without being accompanied by any objective or subjective manifestations or any deterioration of either the general condition or that of the joints. (Figs. 1 and 2, p. 218.)

The appearance of the nodules in some cases goes to prove that they in themselves do not indicate graver types of arthritis, since 7 of these patients were markedly improved by treatment notwithstanding the long duration of the disease. (See Figs. 3 and 4, p. 218.)

As a result of the treatment there was total disappearance of the nodules in 2 patients, and a decrease in the size of the nodules in 6 others. The involution of nodules took place spontaneously in 2 cases. Of the 25 patients exhibiting subcutaneous nodules who received treatment, and who were, therefore, under observation for a long time, the nodules were affected by treatment in 8 (32%).

Comments

Taking as a basis our observations concerning subcutaneous nodules in this group of 55 patients, we are inclined to disagree with the view given by Dawson in 1933, because we have noted that the presence of such nodules has no influence on the prognosis in rheumatoid arthritis. We cannot understand the reasons which induced Dawson, and many others after him, to consider the presence of subcutaneous nodules in rheumatoid arthritis as indicating a poor prognosis. This is the present-day view, and so far the facts upon which it is based have neither been explained nor contested. On the basis of the data reported in this paper, we came to the conclusion that subcutaneous nodules in rheumatoid arthritis are valueless from a prognostic standpoint because they do not signify any cardiac involvement or any more serious type or longer duration of arthritis or its activity, nor do they constitute an obstacle to treatment. *They are, therefore, a somewhat insignificant finding.*

Summary and Conclusion

We hold that the presence of subcutaneous nodules in rheumatic fever denotes a grave prognosis because such nodules indicate carditis and active diseases. This study of subcutaneous nodules in rheumatoid arthritis, however, shows that they do not indicate an unfavourable outlook, any involvement of the heart, or any enhanced activity, intensity, or severity of the arthritis, and that they do not constitute any obstacle to treatment.

These differences in the features of the subcutaneous nodules in the two types of rheumatism constitute just one more factor to prove that rheumatoid arthritis and rheumatic fever are diseases distinct from one another.

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(*For Illustrations to this Article see page 218*)

HYPERSENSITIVITY TO COLCHICINE

BY

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A patient suffering from atypical arthritis of the rheumatoid type was given crystalline colchicine in the usual dose as a diagnostic measure because the possibility of gout had been suggested by the radiological and biochemical findings. Death from colchicine poisoning resulted. In the present paper an attempt is made to assess the significance of this, and of other unusual features of the case.

Case History

A married man, aged 39, gave a twelve years' history of pain and swelling of various joints. These symptoms commenced in fingers and feet in 1934, and in later years the right wrist, knees, hips, neck, and jaws were affected. Since 1941 glandular swellings had been noted in groins and axillae whenever symptoms were severe. These swellings disappeared with improvement in the joints. In January, 1946, all teeth were extracted, and thereafter the left wrist also became swollen and painful. In the first five years of his illness the patient lost weight and was unduly tired, but latterly his weight had been steady. He had no other symptoms apart from epigastric pain two hours after food, readily controlled by dietetic measures. A duodenal ulcer had been diagnosed radiologically.

The only previous illnesses were influenza, pleurisy, and lumbago in 1930. The patient was temperate in his habits. Acute exacerbations of pain were not related to over-indulgence in food or drink. There was no family history of arthritis or gout.

On several occasions courses of gold had been prescribed without benefit. The most recent course had to be stopped after 0·6 g. of myocrysin because of an exacerbation of symptoms in the left wrist. Other treatment, such as paraffin wax baths, " electrical treatment ", and tonsillectomy had not helped him. Although for twelve years the patient had always symptoms in one or more joints he was usually able to continue at work as an upholsterer.

When first seen as an out patient in November, 1946, the patient was a sparely built man with a good colour. There was a moderate degree of swelling and limitation of movement at both wrist joints and at the right ankle. Similar but less marked changes were present in the left first and second metacarpo-phalangeal and proximal interphalangeal joints. No enlargement of lymph glands was detected at this time, and examination of all other systems was negative.

The blood sedimentation rate was 22 mm. in one hour (Westergren), and the blood uric acid was 4·4 mg. per 100 c.cm. of blood. Skiagrams showed destructive changes in the right wrist and in the left thumb and index finger, and soft-tissue swelling of the wrists. Punched-out areas, present in the left index finger and thumb, were suggestive of gout, but the other appearances were those of rheumatoid arthritis (Fig. 1, p. 216).

A provisional diagnosis of rheumatoid arthritis was made. Rest was advised, the right ankle was strapped, and plaster-of-Paris splints were made for the wrists. The alternative diagnosis was gouty arthritis. As a diagnostic test, and because other drugs had been ineffective, it was decided

to try treatment along the lines recommended by Bauer and Klemperer (1944) for cases of gout: 20 gr. each of sodium salicylate and sodium bicarbonate were advised thrice daily in an endeavour to lower the blood uric acid, and it was suggested that colchicine should be tried if an exacerbation of pain occurred.

The patient was seen again five weeks later. He stated that symptoms had continued in spite of rest and sodium salicylate and had steadily increased until three days previously, when pain became severe and he felt hot and tired. Marked swellings were noted by the patient in groins and axillae. On the day before admission to hospital he had begun taking colchicum and mercury pills (B.P.C.) prescribed by his doctor thrice daily, with, he thought, some improvement. Since the patient, however, was still obviously ill and in pain he was admitted to hospital.

On admission the joint findings noted when the patient was first seen were more marked, particularly in the left thumb and forefinger. The left ankle was also swollen and painful. In both groins and axillae there were visible and easily palpable swellings, most marked in right groin and left axilla. The glands were discrete, firm but not hard, and slightly tender. Examination of all other systems was negative.

Temperature was 98·2° F.; pulse 80; respiration 20; haemoglobin 95 per cent.; leucocytes 8,400 per 100 c.mm. of blood; differential count showed no abnormality; urine contained no abnormal constituents; blood sedimentation rate was 52 mm. in one hour (Westergren); plasma uric acid was 4·4 mg. per 100 c.cm. of blood.

As some subjective improvement had resulted from the colchicum and mercury pills prescribed by the patient's doctor it was decided to continue with colchicine until symptoms of toxicity appeared, as recommended by Bauer and Klemperer (1944). Crystalline colchicine (0·5 mg.) was prescribed at two-hourly intervals throughout the day for six doses. Pain in the joints decreased, and this was accompanied by an improvement in the patient's general condition. Blood sedimentation rate fell to 12 mm. in one hour. At 9 p.m. on the third day in hospital, after a total of 6 mg. colchicine had been administered, the patient complained abruptly of nausea and colicky abdominal pain. Treatment with colchicine was immediately stopped. These symptoms were followed by repeated vomiting and diarrhoea, which continued throughout the night and were unrelieved by morphia. On the following morning a moderate degree of shock was present. Vomiting and diarrhoea continued until the afternoon of the fourth day. Intravenous fluids were administered, and the patient's condition improved, but in the evening vomiting returned. Temperature was now 101° F.; pulse 120; respiration 30. During the night the patient became comatose and incontinent. At this stage the urine contained no albumin or urobilinogen, and the blood urea nitrogen was 47 mg. per 100 c.cm. of blood. The patient became more deeply comatose throughout the following day. Pulse and temperature continued to rise, and the patient died on the afternoon of the fifth day in hospital, forty-two hours after the onset of symptoms, three days after the prescription of colchicine in full doses in hospital, and five days after colchicine had been commenced as an out patient.

Autopsy Findings

Macroscopic

The metacarpo-phalangeal joint of the left forefinger, when opened, showed thickening of the periarticular tissues and a roughened appearance of the articular surfaces. Glands removed from the right inguinal, left axillary, and supra-clavicular regions were moderately enlarged, but on section showed no naked-eye abnormality. The other positive findings were the presence in each pleural sac of about 200 c.cm. clear blood-stained fluid; at the apices of both lungs there were some emphysematous bullae, and on section the parenchyma was extremely congested, almost haemorrhagic, and very oedematous; the pericardial sac contained about 10 c.cm. of clear fluid; a few subepicardial petechial haemorrhages were present. No significant naked-eye abnormality was present in brain, meninges, mouth, pharynx, heart, aorta, stomach, large and small intestines, liver, gall bladder, bile ducts, spleen, or kidneys.

Microscopic

Lymph Glands.—Sections of lymph glands taken from left supra-clavicular, axillary, and right inguinal regions showed a similar picture (Fig. 2). The germinal centres showed the greatest changes; these were common to every one examined. There was considerable variation in size of the centres, the largest being about five times as big as the smallest. Some were surrounded by a collar of lymphocytes two or three layers thick. A generalized necrosis was the most striking change. Nearly all of the constituent large lymphocytes were replaced by round particles of darkly staining granular matter resembling pieces of degenerated pyknotic nuclei. A few recognizable but pale ghostly cells and histiocytes were present, but in view of their faint stain probably not viable. Some normal looking lymphocytes were distributed irregularly through the centre. The background consisted of an amorphous, eosinophilic material. The remainder of the gland showed no great changes, but the sinuses were fairly prominent, though empty. The vessels throughout the gland were prominent, dilated, and filled with red cells. No mitotic figures, normal or abnormal, were present.

Joint.—The articular surface of the base of the proximal phalanx of the left forefinger showed chronic arthritis. The articular cartilage was completely absent and replaced by a thick pannus of fibrous tissue. The synovia showed proliferated fingers, which were infiltrated with inflammatory round cells, and contained numerous dilated vessels. Below the articular surface was a zone of normal bone, and below this an area of bone necrosis. In this area there was a loss of cancellous structure which was replaced by a diffuse meshwork of faintly acidophile-staining material containing a large number of polymorphs and some lymphocytes. The picture suggested a small subacute abscess (Fig. 3).

Other Organs.—The section of the lung showed an acutely congested parenchyma. The alveolar capillaries were widely dilated, and engorged with blood. Many small haemorrhages had occurred, and here and there were alveoli within which were pigment containing macrophages. Some oedema was present in most of the alveoli.

The spleen was extremely congested, so much so that it was difficult to determine any pathological change. The malpighian corpuscles seemed to be reduced in diameter due to disappearance of the peripheral lymphocytes. No degenerative or necrotic changes could be seen in the lymphoid structure. Liver and kidney showed cloudy swelling only. Muscle showed no abnormality, in particular no evidence of nodular polymyositis.

Discussion

In toxic doses colchicine causes gastro-intestinal and renal irritation followed by progressive paralysis of the central nervous system. It is converted in the body to an oxidation product probably oxydicolchicine, which is excreted by bowel and kidney, and which in its excretion has an irritative action on excretory organs, possibly by causing capillary dilatation. This toxic action on the capillaries may be widespread and account for the profound shock in some cases. Terminal symptoms are due to the toxic action on the central nervous system.

The excretion of colchicine is slow, so there is a latent period of three or four hours between the toxic dose and symptoms. The main symptoms are nausea, vomiting, abdominal colic, diarrhoea, oliguria, shock, confusion, coma, and death.

Colchicine arrests mitosis at the metaphase, and has been shown to produce a regression in experimental tumours in laboratory animals. For this reason it has been used in the treatment of inoperable carcinoma. Brown and Seed (1945)

describe two such cases treated with colchicine, which died from colchicine poisoning. These authors give the only detailed account of the autopsy findings in colchicine poisoning that we have found in the literature examined on this subject. They conclude that colchicine does not produce distinctive gross changes in the organs; the effects of the drug are visible only on microscopic examination, when arrest of mitosis at an early stage, usually the metaphase, occurs with the production of bizarre and abnormal nuclear configuration frequently leading to cell death. This effect is general and selective only in the same sense that those tissues which have the highest rate of cell division and metabolism are affected first; that is, bone marrow, tumours, skin, lymphoid structure, etc.

The present case is, therefore, typical of colchicine poisoning both in regard to clinical manifestations and autopsy findings. The massive necrosis of germinal centres of enlarged lymph glands is a manifestation of the action of colchicine on rapidly dividing cells. The significance of the lymphadenopathy is discussed later.

Few cases of colchicine poisoning have been described; fatalities have usually been the result either of large quantities of the wine being drunk in error, or of the prescribed dose being multiplied several times by the patient in an attempt to abort a severe attack of pain. Taylor (1934), in reviewing lethal cases, found it difficult to estimate the fatal dose of colchicine, but considered that one grain (64·8 mg.) would be likely to produce fatal effects. Very much smaller doses have resulted in death. Details of these are given in the Table.

TABLE

Case notes	Dose of colchicine	Quoted by
Male, aged 47, took in 1 hour 12 capsules, each containing ¼ mg. of colchicine and 20 gr. of methyl salicylate. Death occurred 10 days later.	3 mg.	Taylor (1934)
Death after drinking 15 c.cm. of tincture	4·5 mg.*	Goodman and Gilman (1943).
Male, aged 39, given approximately 7 mg. of colchicine in 4 days, died 42 hours after onset of symptoms.	7 mg.	Present case (1947)
Death on fourth day after drinking 3½ drachms of vinum	11 mg.	Taylor (1934)
Female, aged 65, with inoperable carcinoma of the right breast, was given 13 mg. of colchicine over a period of four days. Three days of vomiting, diarrhoea, and prostration followed, and death occurred on the seventh day after the first dose of colchicine.	13 mg.	Brown and Seed (1945)

*Goodman and Gilman give the equivalent dose of colchicine as being 6 mg.

In the present case the patient stated he had taken one colchicum and mercury pill (B.P.C.) three times a day for two days before commencing the crystalline colchicine in hospital, representing an additional 0·6 mg. of colchicine. Death,

therefore, occurred after a total of approximately 7 mg. of colchicine had been given over a period of four days.

Bauer and Klemperer (1944) state that hypersensitivity to colchicine is unknown. This statement has been repeated recently by Bauer (1947) and by Fletcher (1947). It will be seen in the Table that five fatal cases including the present one have been reported following 13 mg. or less of colchicine, that is, after a quantity that may be prescribed for therapeutic purposes. It is difficult to explain these cases, and, in particular, the present case, as other than very rare examples of hypersensitivity to colchicine.

In this country colchicine is usually prescribed as the tincture in doses of 20 minims four-hourly. This is equivalent to a daily total of approximately 2 mg. of colchicine. Because of the satisfactory results usually obtained on this dosage, and on consideration of the five fatal cases listed above, the prescription of colchicine in the doses recommended by Bauer and Klemperer must necessarily give rise to considerable anxiety. Accordingly we are of the opinion that if the pure drug is to be used the total dose of crystalline colchicine for the first day should not exceed 3 mg. In view of the delay in excretion of the drug it is advisable that the total daily dose should be divided equally throughout the twenty-four hours. On the first day an initial dose of 1 mg. may be given, and thereafter half a milligramme four-hourly for four doses. On the second and successive days half a milligramme should be prescribed six-hourly. The drug must be withdrawn on the relief of symptoms, or on the first sign of toxicity. The importance of warning the patient not to exceed the prescribed dose is obvious.

Other interesting features of this case are, the finding of a subacute abscess in relation to a joint whose pathology was otherwise typical of rheumatoid arthritis, and the widespread incidence of lymphadenopathy. An unusual opportunity is presented of correlating an exceptional pathological finding with the radiological features (Figs. 1 and 3). The punched-out areas interpreted as being suggestive of gout were presumably due to abscesses. Lymphadenopathy is described as occurring in rheumatoid arthritis, but opinion varies as to its frequency. Enlarged lymph glands were found in 19 per cent. of cases of rheumatoid arthritis by Freund (1929), in 53 per cent. by Coates and Delicati (1931), and in 9 per cent. by Waterhouse (1907). These different figures may be explained by different interpretations of pathologically enlarged glands, or by varying thoroughness in examining cases for this feature (Talkov and others, 1942). The present case was exceptional in that the enlargement of the glands was of such a degree that in the groin they were easily visible. In the writers' experience glandular enlargement of the order present in this case is rare in rheumatoid arthritis. This unusual feature may be explained by the presence of the abscesses in the sub-articular bone of some joints, the significance of which is not clear. It would appear that local infection of undetermined bacteriology and unknown source played a part in the aetiology of the arthritis and probably accounted for the marked lymphadenopathy in this case.

Summary

A fatality following colchicine therapy is described in a case of atypical arthritis of the rheumatoid type.

It is suggested that this is a rare example of hypersensitivity to colchicine. The toxic effects of this drug are discussed and suggestions are made about its dosage.

Other unusual features of the case, marked lymphadenopathy and sub-articular bone abscesses, are briefly discussed, and the pathological and radiological findings are correlated.

We gratefully acknowledge our indebtedness to Professors L. S. P. Davidson and A. M. Drennan for much helpful criticism and advice.

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(*For Illustrations to this Article see pages 216 and 217*)

AGGLUTINATION OF HAEMOLYTIC STREPTOCOCCI (GROUP A) IN SERUM FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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The theory of a streptococcal causation of rheumatoid arthritis continues to be of great importance, and since it was first advanced it has been supported by serological and bacteriological investigations, including agglutination tests, more especially in the United States. Table 1 summarizes a number of these investigations.

The writer (Kalbak, 1946) obtained 79 per cent. of positive reactions among rheumatoid arthritis patients. In the control material the positives represented a very low percentage. In the same year Cecil and de Gara reported finding positive agglutination reactions in 60 per cent. of 268 patients with rheumatoid arthritis. The number of positive reactions among scarlatina patients was only 25 per cent., and in a control material there were none, or only very few. In their opinion the test was more often positive in patients with a severe joint affection, whereas the reaction became weaker and gradually quite negative as the disease improved or was cured.

Edström and Winblad (1947) had 76 per cent. of positive reactions among fifty patients with rheumatoid arthritis. They claimed that the reaction did not become positive until four or six months after the commencement of the streptococcal infection. Using a somewhat altered technique, Thulin (1947) obtained over 90 per cent. of positive reactions, and Hedlund (1947) 55 per cent., among patients with rheumatoid arthritis. The article by Angevine and others (1942) should also be consulted.

The conclusions to be drawn from these investigations appear to be:

1. The agglutination test is best made with haemolytic streptococci of Lancefield's Group A.

2. Among polyarthritis patients there are between 50 and 75 per cent. positive agglutination reactions.

3. The percentage of positives in the control materials is very low.

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* Chief, J. Orskov, M.D.

TABLE 1

Investigators	Year	Antigen	Titre in positive reaction	Patients with rheumatoid arthritis		Control material			
						Str. infections		Normals, and other diseases	
				No. of patients	% + reaction	No. of patients	% + reaction	No. of patients	% + reaction
Cecil, Nicholls, and Stainsby ..	1931	α-Str. " typical "	≥ 640	103	94	—	—	102	2
Gray and Gowen	1931	α-Str. " rheumatoid "	≥ 640	—	62	—	—	—	—
Dawson, Olmstead, and Boots ..	1932	haemolyt. Str.	≥ 160	152	69	49	6	207	2
Keefer, Myers, and Oppel ..	1933	haemolyt. Str. Group A	—	22	55	103	15	176	2
McEwen, Alexander, and Chasis	1935	haemolyt. Str. Group A	—	—	—	—	—	—	—
Dawson and Olmstead	1936	haemolyt. Str. Group A	≥ 160	666	51	—	—	—	—
Goldie	1938	haemolyt. Str. Group A	≥ 200	28	75	—	—	—	5
Packalén	1943	haemolyt. Str. Group A	≥ 160	17	59	10	50	152	11
Cecil and de Gara..	1946	haemolyt. Str. Group A	—	268	60	—	25	—	2
Kalbak	1946	haemolyt. Str. Group A	≥ 40	183	79	147	7	194	2
Edström and Winblad	1947	haemolyt. Str. Group A	40	50	76	—	—	—	—
Hedlund	1947	haemolyt. Str. Group A	40	—	55	—	—	—	—

TABLE 2

Patients with rheumatoid arthritis (241)		
	+ reaction	− reaction
168 patients (various hospital departments)	77%	23%
73 patients (own observations)	79%	21%

The Author's Investigations

Technique

My technique is based mainly upon that of Dawson and Olmstead, though with certain modifications, whereby the reaction has become rather more specific; the positive percentage among rheumatoid arthritis patients has increased, whereas the control material still gives a very low percentage of positives.

A suitable streptococcus is selected, that is, belonging to Group A (though Groups C and G may also be employed). Groups A, C, and G are the so-called human-pathogenic haemolytic streptococci, and it is these that form streptolysin. The type is a subordinate matter. The important point is that the bacterium grows diffusely with no tendency to agglutinate spontaneously.

Culture proceeds in a medium which experience shows will give diffuse growth. The composition of the broth is as follows:

To 750 g. minced beef add 1·5 litres of mains water, and leave overnight in the refrigerator (4° C.). Next day, boil the mixture for 15 minutes, then filter through filter-paper, and adjust the *p*H to 8·0 by adding sodium hydroxide. Boil again for 30 minutes. To 500 ml. of this meat extract add 5 g. peptone (Bacto- or Orthanapeptone) and 2·5 g. sodium chloride. Boil again. Adjust the *p*H to 8·0 by adding sodium hydroxide. Filter into a sterile flask, then autoclave for 20 minutes at 120° C. After autoclaving the *p*H must be about 7·6 to 7·8.

The broth is thus rather thin without glucose. The small quantity of sodium chloride is supposed to have a bearing on the diffuse growth of the bacteria. The kind of peptone is very important in getting a successful result. One requirement is that the streptococci grow very slowly out into the broth, so that even after about 14 hours' growth it is only diffusely turbid. If they grow quickly and strongly, the culture seems to be less suitable as an antigen. Possibly the optimal period of growth varies somewhat for the various strains, but it seems to be more than 10 hours and less than 15.

Having secured a suitable growth, the living culture is used as the antigen and added direct to the serum dilutions. Heat-killed culture can be employed (56° C. for 30 minutes), but this process increases the chances of spontaneous agglutination, so it is better to work with living culture.

The patient's serum is diluted with 0·3 per cent. sodium chloride to 1 : 10–1 : 20, etc., to 1 : 1,280, in eight tubes in all. The same amount of living culture is added, so that the final dilutions are 1 : 20–1 : 40, etc., to 1 : 2,560. After careful shaking, the tubes are left for two hours in a waterbath at 52° C. for agglutination. They are then left overnight in the refrigerator at 4° C., and read next day.

Reading is macroscopic. The tubes should be lightly shaken. The culture will have precipitated somewhat as a result of the long period in the refrigerator. If the reaction is negative the sediment shakes up just as diffusely as the original culture. If it is positive the sediment shakes up in clumps consisting of agglutinated streptococci. The strength of the reaction is indicated in four degrees:

4. Large coherent discs which are difficult to shake to pieces. This reaction is very rare. The supernatant fluid is clear. Signified as ++++.

3. The sediment shakes up in coarse clumps. The fluid clear. Signified as +++.

2. The sediment shakes up in medium and small clumps. The fluid clear. Signified as ++.

1. The sediment shakes up in very small "woolly" clumps. The liquid is turbid, signifying that agglutination is only partial. Signified as +.

0. The sediment shakes up diffuse. No agglutination. Signified as 0.

Negative reactions are: all cases where the agglutination in the first tube is 0 or 1, regardless of the degree of agglutination in the next tubes, for instance: (1) 00000000, (2) 11000000, and

(3) 01210000. It is open to discussion whether agglutination such as (2) should be described as a doubtful positive reaction. In the present work this latter form of reaction is called negative. As strength 2 in the first tube is almost always followed by the weaker strength 1 in the next tube, this means that there will scarcely ever be a positive reaction with a titre of 20, and that therefore the weakest positive reaction will almost always be 1 : 40. The most frequent positive reaction is, for example, 33210000.

I have made a number of tests of the living culture as the antigen, especially when compared with trypsin-treated culture and after washing with 0·9 per cent. sodium chloride. As the living culture will not agglutinate after washing, as all types of haemolytic streptococci can be agglutinated in the serum of polyarthritis patients, and as there is a distinct difference between agglutination with living culture and that with trypsin-treated culture (in which the group antigen is particularly prominent), I believe that the antigen which governs the agglutination in serum from rheumatoid arthritis is a very labile antigen lying on the surface (capsular antigen?) which is neither a type nor a group antigen and which is associated with the human-pathogenic haemolytic streptococci (Groups A, C, and G).

The Clinical Material

The clinical material comprises a total of 1,141 cases, of which 241 were patients with rheumatoid arthritis, and 900 were control cases.

Rheumatoid arthritis patients.—The 241 patients were made up of 168 from whom samples of sera were sent to the State Serum Institute by various hospital departments, and 73 cases of my own. The findings are shown in Table 2, from which it will be seen that in a series consisting of patients with rheumatoid arthritis there were about 80 per cent. positive agglutination reactions and about 20 per cent. negative.

Especially interesting are my own 15 observations with a negative agglutination test. Among them are four typical cases of rheumatoid arthritis in the active phase, with raised sedimentation rate. The fact must therefore be established before going any further that a negative agglutination test occurs in completely typical cases of rheumatoid arthritis, clinically indistinguishable from the other cases with positive reaction. My other negative cases include two cases of polyarthritis psoriatica—the only ones in the series. Two patients with negative agglutination tests had a normal erythrocyte sedimentation rate, and in another patient with a negative test the joint pains had just begun and were very slight. Two had very old joint affections, of sixteen and twenty-eight years' duration respectively. In both cases the affection was inactive, with complete ankylosis of the joints but otherwise without particular discomfort.

One patient had a normal erythrocyte sedimentation rate and very severe epilepsy. Moreover, she underwent hysterectomy three years ago for severe metrorrhagia. The joint affection began a year later and was not quite typical. There was a pronounced tendency to contracture, and she was operated in both palms for very severe Dupuytren's contracture. The joint affection must be described as atypical.

Two other patients had atypical polyarthritis. One closely resembled sclerodermia. The joints had hardly any capsular swelling, but the skin was very tight and the fingers had a tendency to contracture. The other patient may have

had arthritis urica, for the serum uric acid was constantly high and the joint changes were chiefly localized to the principal joints, whereas there were no changes in the fingers.

The cases of rheumatoid arthritis with a positive agglutination test were on the whole typical. It would, therefore, seem justifiable to conclude that among the polyarthritis cases with a negative agglutination test there are relatively more of an atypical nature, with a normal sedimentation rate, with psoriatic polyarthritis, and with old and inactive or very early disease.

Concerning the patients with a positive reaction, four interesting questions arise:

1. Is there a connexion between the titre and the clinical course?
2. At what stage in the disease does the reaction become positive?
3. At what stage does the reaction become negative again?
4. What effect on the reaction has the treatment (especially gold treatment)?

The observations are rather limited in number as yet, and therefore the figures in Table 3 must be taken with some reserve.

TABLE 3

TITRE VALUES

	Agglutination titres					
	1 : 40	1 : 80	1 : 160	1 : 320	1 : 640	
No. of patients with chronic polyarthritis and positive agglutination reaction.	6 (10%)	18 (31%)	19 (31%)	11 (19%)	4 (9%)	58 patients
No. of patients in control material with positive agglutination reaction.	13 (30%)	22 (50%)	7 (15%)	2 (5%)	— —	44 patients

This table shows that most polyarthritis patients have an agglutination titre of 1 : 80 and 1 : 160, but that a considerable number reach a value of 1 : 320 and 1 : 640. In the control material the titre of the positive reactions is distinctly lower on an average, 80 per cent. of them being 1 : 40 and 1 : 80, and there are none at 1 : 640. The evidence thus is that the strongest reactions occur in patients with rheumatoid arthritis. As far as can be judged it will probably also be found that patients with the most severe lesions have the highest titre.

Patients treated with gold were also tested. Within the period of observation (three to four months) there was no sign of any marked change in the titre. In no case did the titre fall to normal values (negative reaction).

We do not yet know definitely if the reaction can become negative. The probability is that it can, because the test was negative in two old wholly inactive cases in the third phase; but as we do not know whether the reactions of these patients were previously positive, this is simply a not improbable hypothesis;

Coburn, too, claims to have observed that in acute rheumatic fever when the joint affection becomes quiescent the reaction becomes negative.

Another question of particular interest is when the reaction becomes positive. Here again to say anything definite would be bold. Apparently some considerable time elapses before it happens—seemingly longer than the two or three weeks it takes for the antistreptolysin reaction to become positive, and in fact for most sero-reactions. Edström and Winblad (1947) have reported on some interesting observations suggesting that agglutinin scarcely forms until four to six months after the onset of the disease. This will detract from the diagnostic value of the reaction; but by repeating the test at intervals of about a month there is a chance of observing that a negative reaction becomes positive.

The Control Material

The control material consisted of 900 people.

(1) Sixty-four normal people volunteered as blood donors. One had a positive reaction (1·5 per cent.).

(2) There were 130 patients with various medical ambulant affections, arbitrarily selected from the blood samples sent in for Wassermann tests from the Medical Policlinic of the Rigs-hospital. Only one of these had a positive reaction.

(3) The streptococcal infection group consisted of patients infected with haemolytic and non-haemolytic streptococci. There were 20 with scarlatina in the third or fourth week of the attack, and none gave a positive reaction. Next, 38 sera were selected with an especially high anti-streptolysin titre ($\geq$ 800). None of these gave a positive reaction either. But among 100 sera from rheumatic fever patients there were 10 per cent. with a positive reaction.

Actually, the only definite infection with non-haemolytic streptococci is the subacute bacterial endocarditis (endocarditis lenta). Nine cases, all verified by repeated positive blood cultures with *Strep. viridans* demonstrated in each case, gave a negative agglutination reaction. This strengthens the supposition that the reaction is specific to haemolytic streptococci. If the reaction were positive in the case of streptococcal infections in general, we should certainly expect it to be positive in a disease like endocarditis lenta, in which there is bacteriaemia and the streptococci occur freely in the blood stream.

(4) As examples of other infectious joint affections I have included 18 cases of gonococcal polyarthritis. None of the blood samples was positive.

(5) A group of patients with "various rheumatic affections" but excluding rheumatoid arthritis consisted of 41 from the Department of Physical Medicine of the Kommunehospital,

Table 4
CONTROL PATIENTS (900)

Diagnosis	No. of patients	Positive aggl. reaction	Negative aggl. reaction
Normal (donors)	64	1·5%	98·5%
Medical affections (ambul.)	130	0·8%	99·2%
Scarlatina	20	0	100%
Sera with A.S.T. > 800	18	0	100%
Rheumatic fever	100	10%	90%
Endocarditis lenta	9	0	100%
Arthritis gonnorrhoica	18	0	100%
Various "rheumatic" affections	41	15%	85%
Medical affections (hospital patients)	500	7%	93%

comprising patients with arthrosis, rheumatic fever, sciatica, poliomyelitis, etc. In this group the reaction was positive in 15 per cent.

Thus it is among rheumatic fever patients and in this latter group that we find the highest agglutination percentage in the control material (see Table 4). As the last-named group includes rheumatic fever patients, this is presumably the explanation of the relatively high percentage of positive reactions.

(6) Finally, there is a group of hospitalized patients suffering from various medical affections, all in the Nørre Hospital. A total of 533 patients were systematically tested with this reaction. Of these, 33 had chronic polyarthritis, and these were accounted for when dealing with this group of patients. Of the remaining 500, a positive agglutination reaction was obtained from 36 (7 per cent.).

The diagnoses in this group cover a wide variety of diseases, but among the patients with a positive reaction one kind of disease is particularly represented: chronic inflammation in the respiratory tract. Of the 36 patients, 14 had chronic infections of this kind (chronic bronchitis, sometimes combined with asthma, unspecific lung infiltration, bronchiectasis, chronic sinusitis, chronic tonsillitis, etc.). In addition, there were 5 cases of cardiac insufficiency with lung stasis. The remaining 17 cases represent various diagnosis.

The Immuno-biological Importance of the Agglutination Reaction

The aetiological value of the reaction depends exclusively upon whether or not the agglutination is specific, that is, whether it is induced by streptococcal antigens or not. If it is unspecific, it is presumably caused by other antigenic substances occurring in patients with rheumatoid arthritis and possibly not necessarily of a bacterial nature.

The two main arguments against the reaction being a specific reaction to haemolytic streptococci are: (1) the apparent contradistinction between the antistreptolysin reaction and the agglutination reaction; and (2) the fact that it has not yet been possible with certainty to cultivate haemolytic streptococci from patients with rheumatoid arthritis.

If we examine the antistreptolysin titre in a large series of patients with rheumatoid arthritis we find that its distribution is exactly the same as in a normal material (Kalbak, 1944, 1946), that is to say, we find only about 10 per cent. of increased values. Thus the antistreptolysin reaction alone provides no basis for attributing the infection of these patients to haemolytic streptococci. Then how shall we explain that haemolytic streptococci agglutinate in the serum of about 80 per cent. of these patients? Surely both reactions are an expression of an infection by these bacteria? Should not both reactions be positive if there were really an infection by streptococci?

This argument is only apparently right. Both reactions are an expression of an infection with haemolytic streptococci, it is true, but each represents two different mechanisms of immunity. The one (the antistreptolysin reaction) is an *antitoxic* reaction; the other (the agglutination reaction) is an *antibacterial* reaction. This means that first and foremost the antistreptolysin reaction is a reflection of the function of the streptococci, their toxin formation in the organism, whereas the agglutination reaction merely expresses the presence of the bacterium itself, dead or living.

Thus the antistreptolysin reaction depends upon two factors: (1) The presence of haemolytic streptococci, and (2) that these streptococci are living and capable of producing toxin (streptolysin). The agglutination reaction depends only on there being haemolytic streptococci in the organism—it seems immaterial whether they are living and highly virulent, greatly attenuated, or even dead. Thus we may quite well imagine the possibility that the streptococci become attenuated so much that their production of toxin ceases and the antistreptolysin reaction becomes negative, whilst the agglutinins are still being produced and cause a positive agglutination reaction. If we compare this with Edström and Winblad's observation that the formation of agglutinin only becomes perceptible after the disease has lasted from four to six months, this will explain the apparent contradictions. Theoretically there is actually no contradiction when the antistreptolysin reaction is negative and the agglutination reaction positive.

TABLE 5

Mode of immunization	*Antitoxin* antitoxic antibodies	*Agglutinin* antibacterial antibodies	Hypothetic occurrence in clinic
Intravenous injection of streptolysin (toxin).	+++	0	No occurrence
Intravenous injection of killed streptococci.	0	+++	Chronic polyarthritis?
Intravenous injection of living streptococci	(+)0	+++	
Subcutaneous injection of living streptococci suspended in semi-fluid agar (artificial focus).	+++	(+)0	Sore throat and attendant affections.

These views may also be supported experimentally (Table 5): (1) When pure toxin is injected intravenously into rabbits (streptolysin, for example), there is a formation of considerable quantities of antitoxin (antistreptolysin). No agglutinin forms, because there are no corpuscular antigens. (2) With the intravenous injection of killed haemolytic streptococci into rabbits no antistreptolysin forms, as streptolysin is formed only by living streptococci. But there is an abundant production of agglutinins, because their formation depends only on the presence of the bacterial body (living or dead). (3) Agglutinins are also formed by the intravenous injection of living haemolytic streptococci into rabbits. Antitoxin formation seems less certain, probably depending upon whether the bacteria have the chance to settle in the organism, perhaps in one or more foci, to produce streptolysin there. The antistreptolysin titre often rises, but in many cases it does not. (4) With the establishment of a focus (subcutaneous injection of living haemolytic streptococci suspended in semi-fluid agar), streptolysin forms in it and there is an increase in the antistreptolysin titre. In this case the bacteria are mostly confined to the spot and the formation of agglutinin seems to be more uncertain.

If we transfer these four possibilities to the bedside—by comparing them with

the occurrence of antibodies in infections caused by haemolytic streptococci, we shall see that hitherto-known streptococcal infections must chiefly be placed under group 4. They are sore throat and its attendant affections, scarlatina, glomerulonephritis, rheumatic fever, chronic tonsillitis, and the like with increased formation of antistreptolysin and with an absence or only a very low production of agglutinin. Groups 2 and 3, on the other hand, come closer to the serological conditions found in rheumatoid arthritis.

Edström and Winblad by means of monthly tests followed the antistreptolysin titre and the agglutination reaction of patients suffering from rheumatoid arthritis. For example, a patient was hospitalized with symptoms of rheumatic fever, and during the subsequent six months developed the picture of a typical rheumatoid arthritis—a course that is not uncommon. It was possible to show how the antistreptolysin titre, which was high at the onset of the disease, fell in the course of the next four months towards normal values. At the onset the agglutination test was negative, but after five months it became positive and thereafter rose to high values (1 : 640). This is a very important observation. It has gradually become generally recognized that an increased antistreptolysin is due to infection by haemolytic streptococci; when a positive agglutination reaction follows immediately afterwards, it is a very strong argument that this reaction, too, is caused by haemolytic streptococci—that in other words the reaction is specific to these bacteria.

The agglutination reaction is associated with the human-pathogenic haemolytic streptococci—groups A, C, and G (and possibly certain streptococci of group E). Other groups do not react. Other streptococci, *Strep. viridans*, enterococci, and other bacteria on the whole, do not seem to react with sera from patients with rheumatoid arthritis.

Starting with the clinical observations, and repeated agglutination tests on individual patients, the following hypothesis may be advanced: *A positive agglutination reaction is an expression of a chronic infection with haemolytic streptococci. If the antistreptolysin titre is simultaneously negative, the indication is that the streptococci have lost their power of producing toxin and are of low virulence.*

The probability is that the antigen (agglutinogen) which governs and assists in the agglutination reaction is situated on the outermost surface of the streptococci and is of a labile nature.

On the basis of the investigations of Lancefield and others, the opinion now is that the antigens of the haemolytic streptococci are arranged in an inner and an outer layer. Inside is the group-antigen C (apparently a complex polysaccharide). Outermost are the type-antigens M and T. M is a nucleoproteid digestible by trypsin. The presence of the antigen T, which is also supposed to be a polysaccharide, is perhaps rather more uncertain. According to my present view, after a period of between ten and fifteen hours' growth in the special broth the streptococci develop a " capsular substance " with antigenic properties and of an extremely labile character. (This antigen might be labelled Y.) If the bacteria

TABLE 6

Washing test with 0·9% NaCl	Agglutination with serum from patient with rheumatoid arthritis
Unwashed living culture	33322100
Living culture washed once	11000000
Living culture washed 5 times ..	00000000

grow too quickly or too long, it is destroyed. Washing experiments show its extreme lability (Table 6). The originally living culture gives a strong positive reaction with a serum from a patient with rheumatoid arthritis; but after being washed once and five times in 0·9 per cent. saline, the reaction falls off distinctly, or perhaps disappears.

This serological reaction is of value to our understanding of the *aetiology* of rheumatoid arthritis. If the reaction is specific (and as yet there is nothing to argue that it is not), it means that haemolytic streptococci play a dominating aetiological role, although it is most probable that there are other aetiological factors in the very complex picture which rheumatoid arthritis presents. We cannot completely explain this affection solely as a simple chronic infection by haemolytic streptococci.

In addition, the reaction brings to light certain interesting points of resemblance between rheumatic fever and rheumatoid arthritis. Several earlier authors have averred that these diseases are related, but this theory only now finds a more tangible basis.

Presumably the agglutination test may also be of some importance in the diagnosis of rheumatoid arthritis. A positive reaction will support the clinical diagnosis, and a negative one should induce the clinician to reconsider it. In suspected cases, where the reaction is negative, the test should be repeated at regular intervals (say once a month). If it changes from negative to positive, the diagnosis is assured. The reaction may also be of some value in cases that are difficult to diagnose (mixed cases of arthritis and arthrosis, atypical polyarthritis or rheumatic fever, vague pains in the finger joints, etc.). Here, as with all other serological reactions, the clinician should remember, however, that a negative reaction does not definitely preclude the disease, and that a positive reaction merely supports the clinical diagnosis.

Summary

Earlier investigations of the agglutination test with streptococci are referred to. The author's own technique is described. Among 241 rheumatoid arthritis patients the agglutination test was positive in about 80 per cent. Among 900 control patients it was positive in only a very low percentage of cases. The immunobiology of the reaction is discussed, and the hypothesis advanced that the reaction is an expression of chronic infection by haemolytic streptococci and is induced by a labile surface antigen (Y).

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THE ACUTE RHEUMATISM REGULATIONS, 1947

As from 1st October, when the Acute Rheumatism Regulations, 1947, came into force in certain areas, all cases of acute rheumatism, including valvular heart disease arising from rheumatism, that occur among children under 16 have to be notified to the local medical officer of health. The districts to which the Regulations, made by the Minister of Health under the Public Health Act, 1936, apply are Bristol, Grimsby, Lincoln, Sheffield, and the administrative County of Lindsey (Lincolnshire). Designed to secure information which may aid in the prevention, early recognition, and adequate treatment of rheumatic heart disease and other types of acute rheumatism, the legislation will remain in force for the next three years.

AETIOLOGY OF FIBROSITIS: A REVIEW

BY

MAX VALENTINE

From a review of systems of classification of fibrositis (National Mineral Water Hospital, Bath, 1940; Devonshire Royal Hospital, Buxton, 1940; Ministry of Health Report, 1924; Harrogate Royal Bath Hospital Report, 1940; Ray, 1934; Comroe, 1941; Patterson, 1938) the one in use at the National Mineral Water Hospital, Bath, is considered most valuable. There are five divisions of fibrositis as follows: (*a*) intramuscular, (*b*) periarticular, (*c*) bursal and tenosynovial, (*d*) subcutaneous, (*e*) perineuritic, the latter being divided into (i) brachial (ii) sciatic, etc.

Laboratory Tests

No biochemical abnormalities have been demonstrated in fibrositis. Mester (1941) claimed a specific test for "rheumatism", but Copeman and Stewart (1942) did not find it of value and question its rationale. The sedimentation rate is usually normal or may be slightly increased; this is confirmed by Kahlmeter (1928), Shackle (1938), and Dawson and others (1930). Miller and Gibson (1941) found a slightly increased rate in 52·3% of patients, and Collins and others (1939) found a (usually) moderately increased rate in 35% of cases tested.

Case Analyses

In an investigation Valentine (1943) found an incidence of fibrositis of 31·4% (60% male) at a Spa hospital. (Cf. Ministry of Health Report, 1922, 30·8%; Buxton Spa Hospital, 1940, 49·5%; Bath Spa Hospital, 1940, 22·3%; Savage, 1941, 52% in the Forces.) Fibrositis was commonest between the ages of 40 and 60; this is supported by the Spa Hospital Report, Buxton, 1940. Among the under forties it was commoner in females, the reverse being the case in the over sixties. Radiological changes were found in 50% of men and 80% of women examined, and there was a familial tendency to "rheumatism" in 23% of cases. In men the sciatic site was the commonest affected. (38·8%) followed by the lumbar area, shoulder girdle, and periarticular regions, 18·8, 17·2, and 15·5% respectively. In women the sciatic site was affected in 25·4%, the figures for the other areas being 18·6, 23·6, and 18·6%. Jews formed 3% of all patients in the consecutive series of 481 cases, and of these 85% had been diagnosed as suffering from fibrositis.

Bacteriological Theories

Llewellyn and Jones (1915) collected a large amount of material from very scattered sources and concluded that there were primary and secondary factors in the production of fibrositis. The primary causes they took to be either bacterial or auto-intoxicative; they alleged that most fibrositic subjects suffer from focal sepsis, and that some of them improve dramatically after this has been eradicated, and also following the use of autogenous vaccines or colonic wash-outs with the Plombière technique. The experiments of Goadby and of Rosenow are quoted,

whereby the lesions of " rheumatic myositis " were produced in animals by the inoculation of a streptococcal strain. Collins (1940), however, thinks that animal experiments are unlikely to be helpful in elucidating the cause of human fibrositis, which is essentially a subjective phenomenon, and draws attention to the difficulty of deciding whether experimentally produced lesions may not have been brought about by other causes, e.g. incidental trauma.

This view, that the majority of fibrositic subjects suffer from focal sepsis, does not now meet with general agreement (vide Douthwaite, 1940; Slot, 1940; Collins, 1940; Savage, 1941; Ellman and others, 1942; Valentine, 1943) and the results of removing any foci present are frequently disappointing (Gordon, 1940; Slot, 1940); colonic lavage and the use of autogenous vaccines have now been for the most part abandoned. Crowe (1926) claimed good results in all types of " rheumatism " with vaccines, but it is seldom that a patient's improvement can be attributed directly to such treatment. Vaccines are often prepared from septic teeth, but the work of Fish (1943) shows that there is comparatively little absorption from septic teeth, as the inflammatory area becomes walled off. There is more toxic absorption from gingivitis. Another point is that any tooth will produce a growth (usually mixed strains of *Strep. viridans*) on a culture plate, unless the gums were previously cauterized, because non-sterile saliva is forced between the tooth and the peridontal membrane in the process of extraction. This is another fact casting doubt on the value of such vaccines. Vaizey and Clark-Kennedy (1939) have also questioned the widely-accepted relation between dental sepsis and the rheumatic diseases. However, there are occasional cases which appear to justify vaccine treatment, such as the one quoted by Myers (1939).

The theory of sub-infection put forward by Adami is also cited by Llewellyn and Jones (1915) as a possible cause. According to this hypothesis, bacteria are carried in the blood stream from septic foci or from the alimentary tract, and produce chronic interstitial fibrositis without setting up suppuration. This is stated to be brought about by the proliferation of connective-tissue elements caused by the endotoxins released upon lysis of the bacteria. According to more modern investigations, however, toxins usually enter the system via the lymphatics, and such bacteria as enter the blood stream are, unless in the case of an overwhelming dose, destroyed in quite a short time by the leucocytes. Auto-intoxication was also advanced as a possible cause, but need not further be discussed.

Secondary or exciting factors Llewellyn and Jones (1915) state to be low temperature, excessive or deficient muscular exercise, and the influence of occupation or strain. The same writers include traumatic fibrositis in their classification, but reserve it for cases in which direct injury plays an obvious part, as in muscular strains and tears.

Five years after the publication of the work of Llewellyn and Jones, Stockman (1920) distinguished (i) original causes, including acute rheumatism, rheumatoid arthritis, sore throats and influenza, gonorrhoeal septicaemia, mucous colitis, and chronic *B. coli* infections of the bladder; and (ii) subsequent attacks, precipitated by exposure to cold, or damp, unusual or violent muscular exercise, acute indigestion, and slight febrile attacks.

Hypersensitivity to Diet

Thomson and Gordon (1926) regard strain and exposure to chill as contributory causes, and postulate as the essential feature of fibrositis a toxin, derived usually from the colon or from focal sepsis. In support of this view they put forward the questionable statement that fibrositic subjects possess a functional inferiority of the lower digestive tract and are particularly liable to gastro-intestinal disorders.

Writing of lumbago, Llewellyn (1927) makes out a case for hypersensitivity to certain protein foods, and invokes a similar explanation for the action of septic foci, viz. one transient bacteriaemia sensitizes the system, and a second produces an anaphylactic reaction, of which the lumbago syndrome is a symptom. In the same article he stresses the importance of trauma in the history of lumbago, and also makes one of the earlier references to vasomotor defects in the rheumatic diseases. Such infective theories have been criticized by Douthwaite (1938), who considers that deep massage might be expected to worsen the condition rather than improve it, as it does in actual fact, were the tissues invaded by bacteria. Collins (1940) finds that painful states of muscle and connective tissue may result from toxaemia or septicaemia, but does not consider that fibrositis comes under this category at all.

Hypothyroidism

Douthwaite (1938) criticizes Llewellyn's suggestion of a subthyroid state as being an important precursor of chronic rheumatism, stating that if any abnormality exists in fibrositis it is more likely to be hyperthyroidism. This criticism is in part supported by the investigations of Potter (1938), who found " no great degree " of hypothyroidism in the majority of ninety female cases of chronic rheumatic disorder. In general, the state of the thyroid seems to have little influence in fibrositis.

Vascular Deficiency and Metabolites

Copeman (1933) mentions sensitivity to diet and possibly to bacteria or their toxins ; also the poor adaptability of the skin capillaries to changing atmospheric conditions, with secondary accumulation of metabolites and effusion of serum. He also mentions chronic strain, and stresses the importance of fatigue. Douthwaite (1938) criticizes this suggestion of allergy and considers that fibrositis differs too much in its onset and course from the proved allergic diseases to be considered in the same category. Ray (1936) holds similar views to Copeman, mentioning capillary stasis, sensitivity to articles of diet, and chronic postural strain. Also discussing the metabolic factor, Gordon (1936) expresses the view that in the inefficient circulation, metabolites will tend to collect in fibrous tissue, this being relatively less vascular, especially in parts where the greatest muscular activity occurs.

Reconciliation between the infective and metabolic schools is attempted by Patterson (1938), who postulates an infective " seed ", which for implantation depends on suitable " soil " prepared by metabolic processes and endocrine constitution. He also makes an early reference to psychological factors, claiming the importance of over-work or mental strain.

Physiological Reports

At this point the work of physiologists may be considered ; Lewis (1932) has suggested the elaboration of a pain stimulant, which he calls the P-factor, in the ordinary course of muscular activity. This is normally removed in the blood stream but persists in the ischaemic conditions. The P-factor seems to depend directly on the state of the local circulation ; if ischaemic muscles are exercised, pain is produced, the pain remains constant if the exercise is stopped and the

ischaemia maintained, and the pain disappears rapidly when the circulation is restored. Regarding the origin and distribution of pain, Kellgren (1939) observes the effects of stimulation of interspinous ligaments, and states that whether pain is segmental or local depends on the depth at which the tissue is stimulated, rather than on the nature of the tissue. According to Samson Wright (1939), fatigue from activity is not due to increase of the H-ion concentration nor to lactic acid. Pemberton (1935) mentions experiments not indicating any abnormal production or disposal of lactic acid in patients with arthritis. Pennington (1939) found increased lactic acid in the sweat after exercise in 100% of cases, and argues from this that there is strong presumptive evidence for the pathological identity of fibrositis with physiological fatigue sequelae in muscles.

These reports in general do not suggest any marked alteration of lactic acid metabolism in rheumatic disorders, and, should any local alteration be found, it will probably be secondary to local vascular deficiency. There is insufficient evidence to show whether this capillary defect is primary.

Gouty Fibrositis

Although the term " gouty fibrositis " is rarely used now, there is some support for the idea that fibrositis may on occasion be associated with an increased blood uric acid. Buckley (1940) mentions cases of this type and considers they should be treated on the same lines as the more common types of gout.

Myalgia and Epidemic Myalgia

Myalgia is defined by Good (1942) as " a muscular disease localized in well-defined parts of the muscle and in its appendages—tendon, ligaments, perimysium, fascia—corresponding anatomically to the origin, insertion, the course or the edge of the muscle ". It thus appears to be essentially a fibrositic lesion.

Epidemic forms have been described of diseases bearing, in their symptoms at least, some resemblance to the condition which we ordinarily recognize as " rheumatic fibrositis ". An epidemic form of brachial neuritis has been described by Wyburn-Mason (1941). He considers that there may be infection by a neurotropic virus, or an allergic reaction to infection, but thinks it unlikely that this is a " fibrositic " condition. Houghton and Jones (1942) describe a series of cases of persistent myalgia following sore throat. They suggest as a cause an unidentified myotropic strain of virus. Douthwaite (1937) quotes a report by Massell and Solomon (1935) of an epidemic of benign myalgia of the neck. It was unilateral affecting mainly the trapezius muscle. It usually lasted two or three days, and deep massage was the best cure. Beeson and Scott (1941) described epidemic myalgia of the neck, with an attack rate of 17·8%. It was commoner in women, and resembled acute fibrositis rather than Bornholm disease. Trail (1943) doubts whether such a disease as epidemic myalgia exists and does not consider it a disease entity. Beeson and Scott (1942) made very thorough investigations on 125 cases of epidemic myalgia of the neck and shoulders, and commented on their results with admirable precision and restraint. The sedimentation rate was not increased in any cases, but a few showed slight pyrexia or lymphocytosis; a history of common cold at the time of onset of the complaint was obtained in 41% of cases, and the myalgia was always worsened by exposure. Washings from the nose and throat of patients failed to reproduce the disease in other persons; transfusions of whole blood from patients, however, reproduced the myalgia in a significant proportion of volunteers, and reasons are advanced to explain failures of transmission.

The largely subjective nature of the complaint makes the assessment of the experiment difficult, but the disease is from all accounts dissimilar to fibrositis.

Subcutaneous Fibrositis

This term is rather loosely applied to superficial tenderness of a fibrositis-like type, which the writer has found common at the nape of the neck and around the scapula. Llewellyn and Jones (1915) mention this type of subcutaneous tenderness, occurring alone or in association with muscle-sheath fibrositis, and Stockman (1928) reserves the term panniculitis for a type of chronic inflammation of the areolar tissue of the panniculus adiposus, mentioning that subjects might be quite healthy in other respects, and that excessive fat or myxoedema were not essential features.

Panniculitis has a different significance for several other writers, who consider it in association with endocrine disease or pathological obesity. Ray (1936) blames endocrine factors, especially hypothyroidism, and states that it is difficult to distinguish from Dercum's disease (see Bochroch, 1902), Thomson and Gordon (1926) state that all cases are hypothyroidic, and Llewellyn (1927) speaks for a similar association, while Buckley (1940) also suggests an endocrine basis.

The Fibrositic Nodule

The fibrositic nodule is by no means universally recognized to exist, and those who do recognize it do not always distinguish different types.

The fibrositic nodule was described by Stockman (1920) as an inflammatory hyperplasia of connective tissue in patches, containing numerous fibroblasts and a sero-fibrinous exudate ; it is swollen, painful, and tender, tends to contract, and can be massaged away. Collins (1940) who has examined some of Stockman's sections, is convinced that no deductions concerning the cause of the nodules can be drawn from them.

Nodules were demonstrated by Collins (1939) in a case of traumatic tenosynovitis showing collections of lymphoid cells in the synovial villi of the tendon sheath. In another case Collins (1940) described a traumatic patellar tendon nodule showing central degeneration, lymphocyte cuffing, and lymphorrhages, but no intense fibroblastic reaction. He comments that traumatic causes may explain histological infective inflammations. Possibly lymphocytes are attracted to the site by the products of cell autolysis.

Elliott (1944) describes nodules, clinically similar to those found in fibrositis discovered in the leg muscles of cases of sciatica with prolapsed discs. Gordon (1940) declares the nodule to be the hallmark of the fibrositic subject but the tombstone of the fibrositic attack, and Copeman (1943) suggests that chill, trauma, and focal sepsis may reactivate nodules which have lain dormant since their inception during previous acute infections.

Fatty nodules are described by Collins (1940). Those had been diagnosed by physicians as " typical fibrositic nodules " and proved to be fatty masses, similar to those described by Stockman (1920) in panniculitis. Copeman and Ackerman (1944) describe oedematous fatty lobules whose removal resulted in the cure of painful tender nodules of the back. Copeman and Pugh (1945) demonstrated nodular fatty lobules enclosed within fibrous walls in the subcutaneous tissues, which constituted trigger points for fibrositic pain. These fat-herniae are considered liable to a type of non-inflammatory oedema with the production of pain

and tenderness; this is the rationale of the dehydration therapy suggested, which is carried out by restriction of fluid intake and intravenous injection of hypertonic saline. Considerable improvement was noted in a statistically significant number of cases in the fairly small series treated.

Areas of muscular spasm have been described by Llewellyn and Jones (1915) as typical of fibrositis; cases may show spastic patches about an inch in diameter, commonly in the trapezius, latissimus dorsi, and sacrospinalis. Elliott (1944) describes a " nodule " which proved under anaesthesia to be localized muscle spasm. This, however, is regarded by Copeman and Pugh (1945) to be a reflex response to irritation from a pathological process situated in tissues outside the muscle.

Collins (1937) describes the pathology of nodules found in rheumatoid arthritis and in acute rheumatism. He is not prepared to accept a common aetiology for the two types.

Postural and Occupational Stresses

Considering sciatica from an orthopaedic standpoint, Wesson (1938) contends that sciatic pain is referred pain from lumbo-sacral muscles, ligaments, and joints, usually from postural imbalance or occupational causes, and that it may only appear in states of anxiety and ill health. Cochrane (1938) argues from the infrequency of sciatica in childhood that it is only when the muscular support of the lower back is strained, or weakened by wear and tear, that lumbo-sacral anomalies and lumbar or sciatic pain occur. de Seze (1939) holds that sciatic pain is mainly caused by discogenetic disease of the space between the fourth and fifth lumbar vertebrae, brought about by deficient musculature of the abdominal wall consequent upon man's assumption of the erect posture.

Comroe (1941) puts forward an American point of view in holding responsible chilling of a part of the body previously over-heated, and trauma, either in the form of injury or chronic strain.

Weil (1939), the French authority, takes the view that continued strain, as indicated by the word " microtraumatisme ", is the main cause of fibrositis. He regards infection as unimportant, but postulates an individual predisposition of an endocrine or sympathetico-vascular type, accompanied by abnormalities in the blood chemistry. The relation between rheumatism and occupational trauma has been dealt with in an interesting article by Duvoir and Desoille (1936), who demonstrate that certain trades cause distinctive types of rheumatic disability. Most French writers, although laying stress on the occupational factor, think there is an underlying individual susceptibility in addition.

An interesting aspect of this question is the development of chronic rheumatism in workmen using pneumatic tools (Wessenbach and Francon, 1938; Copeman, 1940). In this country, Slot (1940) has shown that fibrositis affects those parts of the body which bear the brunt of the occupational strain; for instance, the neck muscles are affected in market porters who carry heavy weights on their heads; whereas in bus conductors, locomotive firemen, gardeners, and dustmen

the muscles of the arm and hand are often affected. Also, at the end of the last century, Arbuthnot Lane drew attention to the influence of occupation in determining the physical constitution of the individual. Van Breemen (1937) has also lent his support to this discussion, but remarks upon the difficulty of deciding if such cases can receive compensation under the existing regulations.

A high proportion of miners with fibrositis was found by Buckley (1933); and Savage (1941) states that most of his cases of fibrositis in the Services occurred in ex-miners. The high proportion of cases of fibrositis admitted to the Buxton Spa Hospital may be accounted for by the mining districts nearby. Conybeare and Glover (1938) stress the influence of occupation in causing postures favouring fibrositis, and the Buxton Hospital Report (1940) shows fibrositis to be commonest in outdoor labourers and miners.

Psychological Factors

Interest has recently been shown in the psychological components of fibrositis. Gordon (1940) distinguishes three varieties: (1) when pain is used as a symbol of emotional discontent; (2) when the whole sensorium is over-sensitized as a result of acute emotional disturbance; (3) when chronic emotional disturbances produce endocrine and autonomic disturbance through vegetative controlling centres in the hypothalamic region which are followed by fibrositis. He quotes cases illustrating the production of fibrositic symptoms by these types of psychological disturbances. In an investigation by Ellman and others (1942), 23 out of 50 patients diagnosed as fibrositis showed no physical abnormality.

Lindstedt, whose teaching has influenced the Scandinavian school, apparently thinks it impossible to overestimate the importance of the psychogenic aspect. Writing principally of sciatica (1938), he states that there is a depressive and psychoneurotic disposition in most cases. A person of this type is hypersensitive to pain, especially when he is over-fatigued from general constitutional causes. Thus muscular strain from faulty posture, working conditions, or from slight congenital or acquired deformities of the lower limbs such as lumbo-sacral anomalies, flat-foot, etc., will produce pain of a sciatic type; or sometimes muscular imbalance alone, without psychoneurotic tendencies, will give rise to pain. The tenderness in the leg, he says, is muscle tenderness, and is not due to neuritic irritability; similarly, he considers that the pain produced by Lasegue's sign is not from stretching the sciatic nerve, but from stretching the tender muscles.

In this connexion the writer suggests the following classification. First, conversion hysteria covering cases with fibrositic-like symptoms but with no physical signs or pathology; the symptoms serving a purpose not directly related to their type. This group also includes cases of fibrositic-like pain occurring as a hypochondriacal conversion in the course of an anxiety state, and cases in which the pain of a former or recent attack is reproduced or perpetuated as a hysterical manifestation. Second, psychosomatic fibrositis, some basis of fibrositis being unconsciously magnified, and to some extent representing the conflict, e.g. pain representing a feeling of injustice, and advanced as a reason for reparation.

There seems to be some justification for a third though uncommon group in which massive and generalized symptoms of fibrositis appear as the main and perhaps only manifestation of a neurosis, possibly from functional vascular and toxic causes. Mention is made of this type of case in the next paragraph.

The Peripheral Vascular System

The vascular changes in fibrositis have lately received much more attention. Pemberton and Pierce (Pemberton, 1935) found dysfunction of the smaller vessels of the skin in arthritis, and Pemberton believes that closed capillary areas play an important part. Bisset and Woodmansey (1932), after photographing capillaries in normal and arthritic subjects, reported spastic capillaries in most cases of well-established rheumatic conditions. Pemberton (1935) also quotes experiments by Rhumann, who found capillary abnormalities, including a slow and interrupted flow, in 70% of patients with muscular rheumatism. Pemberton goes on to describe animal experients by Goldhaft and himself, whereby arterial ligation, or venous stasis, produced bony proliferative changes.

The capillary spasm alleged to be present in fibrositis might be explained on the grounds that, owing to unfavourable or fluctuating conditions of temperature or humidity, the peripheral circulatory reflex protests against such abuse by refusing to function, or at least to function well. If, then, there is an angio-spastic state of the capillaries in fibrositis, it is possible that the osteophytosis which is fairly commonly found in chronic fibrositics is a function of the tissue ischaemia. The theory of halisteresis is no longer acceptable: only bone cells can elaborate or absorb bone matrix (Newton, 1939); venous stasis, with its retarded evacuation of waste products, would probably act as an irritant and cause deposition of bone (Fish, 1943). The typical picture of the capillaries in fibrositis is not of venous stasis, but of narrow, spastic vessels, some being closed altogether (Valentine, 1943). Possibly this could also bring about collections of metabolites such as would stimulate the embryonic resting osteoblasts found in fibrous tissue, with the resulting formation of osteophytes. Another theory might be that, if there is any connexion between fibrositis and osteophytosis, perhaps both fibrous tissue and bone are affected by the same vascular causes and react as their tissues are constituted; the fibrous tissue undergoing the changes leading to the production of fibrositis, and bone tissue producing osteophytes, much as Muir (1924) has put the case in osteo-arthritis. An attempt to discover whether any support could be found for these theories by the examination of case-records of fibrositis proved abortive, as many cases had not been radiographically examined on their first admission to hospital, and others had to be disqualified owing to the "wear and tear" osteophytosis found in most individuals after 55 years of age. It was thus impossible to say whether the fibrositis had run *pari passu* with osteophytosis (Valentine, 1943).

At present there is little or no support for the theory of primary vascular dysfunction in rheumatoid arthritis at least. Collins (1938) takes the view that these vascular phenomena are secondary to the joint disease, and in a further paper he and his co-workers (Collins and others 1939) state that the defect of vascular function is not an essential condition nor the cause of rheumatoid arthritis, but merely an inherent disability of certain subjects leading to aggravation of symptoms.

In cases of acute and fairly superficial fibrositis, pressure over the tender areas causes the appearance of a red flare similar to that produced by the local inoculation of histamine (Valentine, 1943). This phenomenon is often remarked during diagnostic palpation of the tissues, and does not occur, or at least not to the same extent, over unaffected areas. This leads one to think that the release of H-substance or histamine in regions affected by fibrositis might be a compensatory mechanism on the part of the body, designed to increase the sluggish circulation of the affected parts. The treatment of rheumatic complaints by histamine cataphoresis has received some attention (Copeman, 1935; Potter, 1935) and it is of interest to note that Kling (1934) found beneficial results from this line of treatment in the rheumatic group only in "myositis". Another interesting point is the low blood pressure sometimes found in generalized fibrositis. It is con-

ceivable that this is due to the mass release of " H-substance " in the manner suggested above, and similar in nature to, but milder, than the histamine shock described by Lewis (1927).

Eclectic Views

Telling (1935) postulates a complex aetiology but stresses chronic trauma, septic and toxic influences, and climate. Gordon (1940) suggests that fibrositis is a tissue reaction to a number of pathological causes, and Harman (1940) notes that the symptom of pain from deep fibrositis is similar to that from any lesion in a like situation (see also Kellgren, 1938, 1942). Fibrositis might also conceivably be a pattern reaction with a number of triggers, as Fletcher (1939) suggested was the case in osteo-arthritis. In view of its varying pathology, Collins (1940) has drawn attention to the need for fibrositis to be defined afresh in clinical terms, and stresses the diversity of underlying causal conditions.

Fibrositis seems to emerge as an inflammatory tissue reaction, largely from mechanical and physical and sometimes toxic causes. Some defect of circulatory functional response, probably in the peripheral reflex arc, may also render the individual more liable to fibrositis. For convenience the disease may be divided into two groups—the type apparently brought about by physical agencies, such as chronic strain and chill, and that caused by toxic influences such as influenza, gout, acute rheumatism, or focal sepsis, often showing a preference for tissues already damaged by physical means.

Summary

The classification of fibrositis in use at the Bath Spa Hospital is recommended; no diagnostic laboratory tests are of value in fibrositis; an analysis of case records is presented; epidemic myalgia appears to be a separate disease entity; subcutaneous fibrositis differs from the usually accepted meaning of panniculitis; the pathology of the fibrositic nodule is discussed; the role of the peripheral vascular system in fibrositis is considered important; from a discussion on theories of the causation of fibrositis by bacterial toxins, metabolites, postural and occupational stresses, and the psychological factors of the disease, fibrositis is considered to be a tissue reaction, of varying pathology, to several causal factors.

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FIRST EUROPEAN CONGRESS OF RHEUMATOLOGY

Four hundred delegates, representing twenty-five countries, met in Copenhagen from September 3 to 8, 1947, at the first European Congress of Rheumatology under the presidency of Prof. C. Holten of Aarhus. Guests of the Congress were also present from Egypt, America, and Canada.

At a meeting held before the Congress, a European section of the International League against Rheumatism was formed on the same lines as the Pan-American section established during the war. Dr. M. P. Weil of Paris was elected the first President, and Dr. W. S. C. Copeman (Great Britain) and Prof. B. Prusik of Prague Vice-presidents: the Secretary-General and Secretary are respectively Prof. E. Jarlov and Dr. K. Kalbak, both of Denmark. It is hoped that the next Congress of this body will be held in Prague in the coming year.

At the opening session, in the great Town Hall, H.M. the Queen of Denmark was represented by H.R.H. Princess Caroline Mathilde.

In his inaugural address the President referred to the public interest in this group of diseases and the demand for action. To aid in this respect was the object of the new body; it aimed at the exchange of current knowledge between the countries interested and the organization of team investigation in every country through their National branches.

The outstanding contribution in the session which followed was that of G. D. Kersley (Great Britain) on the morbid anatomy and histology of rheumatic lesions. He confirmed the work of Freund and others in 1946 as to the existence of a specific type of lesion in rheumatoid arthritis which occurred in any or all of the muscles of the body at any stage of the disease, as well as in other mesodermal tissues and around the peripheral nerves. The lesion consisted in a perivascular accumulation of lymphocytes with degenerative and proliferative changes in all the coats of the small blood vessels and degenerative changes in the muscle fibres. He also spoke of nodule formation in various types of rheumatism; he suggested the probability of a dual pathology in "fibrositis".

The majority of the scientific contributions dealt with the question of the anti-streptolysin titre and similar antibody responses in both rheumatic fever and rheumatoid arthritis; notable amongst these were the papers of Winblad (Sweden), Kalbak (Denmark), and Svartz (Sweden). Jonsson and Palmborg (Sweden) submitted a valuable critical study, another outstanding contribution coming from van Dam (Netherlands).

The next session under the chairmanship of W. S. C. Copeman (Great Britain) was devoted to the treatment of rheumatoid arthritis by means of gold salts and chemotherapy. This was introduced by a useful contribution by O. Steinbrocker (U.S.A.). A full exposure of the subject by Forestier was presented by Coste (France), and confirmation of the value of various gold salts in rheumatoid arthritis came from papers by both Secher and Clemmeson (Denmark), Sunderlin (Sweden), Kuipers (Holland), and Dobelie (Switzerland). Much less optimistic accounts came from Schlesinger (Great Britain), who was speaking principally of Still's disease, and from some speakers in the discussion. New work reported by Svartz (Sweden) on treatment of arthritis with sulphonamides still awaits confirmation.

The third and fourth sessions, under the chairmanship respectively of F. Coste (France) and van Breemen (Holland), dealt with various aspects of the social background of the rheumatic diseases and with the outstanding biochemical problems of rheumatism. In the former category important statistics were produced from France, Sweden, Switzerland, Denmark, and Eire, whilst under the latter heading papers were read by Delore and Milhaud (France), Edström and others (Sweden), and Dirisu (Turkey). Papers, which were limited to ten minutes, were also presented on various other subjects by a number of delegates including representatives of Belgium, Switzerland, and Czechoslovakia. Steinbrocker (U.S.A.) gave an important paper on the shoulder–hand syndrome in reflex dystrophy of the upper extremity.

The Congress then moved from Copenhagen to the University of Aarhus on the mainland; here it split up into two sections, where reports of personal investigations into various aspects of rheumatism were briefly presented. These included liver tests in rheumatism, studies in the peripheral circulation of rheumatic subjects, food allergy in rheumatoid arthritis, dental infection and joint disease in mediaeval Denmark, rheumatic fever amongst the partisan forces of Yugoslavia, jaundice as a "rheumatic" disease in Poland, and the role of wound sepsis in unmasking rheumatic syndromes during the war in Rumania.

ABSTRACTS

[The abstracts are divided into the following sections: acute rheumatism; articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); gout; non-articular rheumatism; general articles. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. Not all sections may be represented in any one issue.]

Acute Rheumatism

Rheumatic Fever and Rheumatic Heart Disease in the North African and Mediterranean Theater of Operations, United States Army. BLAND, E. F. (1946). *Amer. Heart. J.*, **32**, 545.

A survey was made of the incidence, clinical features, and disposition of rheumatic fever and rheumatic heart disease in Army personnel in the North African and Mediterranean Theatre of Operations from the original landings in November, 1942, to the end of hostilities in May, 1945. Approximately 1,400 patients were admitted to hospital, of whom probably rather more than half had active rheumatic fever, and rather less than half an inactive form, usually with mild rheumatic valvular disease. About half the group with active rheumatic carditis appeared to have developed it on overseas service. Rheumatic fever and rheumatic heart disease accounted for only 3·9% of over 30,000 patients invalided back to the United States from this war zone. It is concluded that measures in force in the American Army to exclude from foreign service those with chronic valvular disease and those especially susceptible to rheumatic fever were highly effective. *E. B. Reeve.*

Capillary Fragility in Rheumatic Fever. MONTGOMERY, H. (1946). *Nav. med. Bull., Wash.*, **46**, 1708.

Vascular symptoms—epistaxis, purpura, and erythemata—are common in rheumatic fever; in fact, according to the author, the chief manifestations of the disease may be predominantly vascular. He uses the term "capillary fragility" for "minute vessel permeability to red cells". The fragility was measured by the appearance of petechiae within 15 minutes of the application of a blood-pressure cuff with a pressure of 100 mm. mercury. If petechiae appeared within 8 minutes the fragility was noted as markedly increased.

The subjects—all of whom were men or women in the Forces—were divided into three groups: (1) controls—those considered to be well or suffering from diseases in which fragility is expected to be normal; (2) convalescent rheumatic fever patients; (3) convalescents from rheumatic fever, but with spontaneous purpura. Of the 25 patients in the first group, 12 gave positive results within the 15 minutes; the average was 11 minutes, and one reacted in 4 minutes. Of the 27 in the second group, 21 were positive within an average of 10 minutes. The author subdivides these into 11 who had sedimentation rates above 10 mm. per hour, 10 of whom were positive within an average of 9 minutes; and 9 who had sedimentation rates below 10 mm., of whom 6 were positive within 11 minutes on an average; of 7 with no recorded sedimentation rate, 5 were positive in from 4 to 15 minutes. Group 3 comprised 19 patients, and the tourniquet test was positive in 17, the average time being 7 minutes. On some of this group other blood examinations were carried out. Platelet counts in 5 patients ranged from 145,000 to 416,000 per c.mm.; the prothrombin time was normal in all. In 7 the bleeding and clotting times were estimated; the former varied from 3 to 5 minutes, the latter (the capillary method was used) from 1½ to 6 minutes. Six patients with marked fragility were treated with hesperidin (vitamin P), 0·5 g. orally three times a day for 10 to 14 days, but no benefit could be observed. The author concludes that the evidence afforded by the above findings favours the theory that rheumatic fever is a disease of the blood vessels.
H. Harold Scott.

A Study on the Incidence of Allergy in Children with Rheumatic Fever. RITTWAGEN, M., ROMANO, F. J., and SVIGALS, M. P. (1946). *Arch. Pediat.*, **63**, 639.

The authors attempted to determine whether the rheumatic child is, as a rule, an allergic individual. Of 100 rheumatic children it was found that 33 gave a history of allergic manifestations and a further 31 a history of allergy in parents or siblings. In a control group of 100 non-rheumatic children, 8 children and 10 families had an allergic history. Whereas only 3% of the population suffers from hayfever, this condition was found in 21 of the rheumatic children; similarly there was a higher incidence of food-sensitivity, vasomotor rhinitis, and bronchial asthma in the rheumatic children than in the general population.
W. Tegner.

Follow-up Study in Rheumatic Subjects Previously Treated with Prophylactic Sulfanilamide. BALDWIN, J. S. (1947). *J. Pediat.*, **30**, 67.

Prolonged sulphonamide therapy in the prophylaxis of recurrences of rheumatism has been extensively used in America and favourably commented upon. Between 1941 and 1946 a group of 55 individuals, all of whom had had prophylactic sulphonamide for 1 to 3 years following some manifestation of rheumatism, were studied for further periods of 1 to 5 years. Thirty-nine had no recurrence, while 16 developed active rheumatic fever. "The higher percentage of recurrences developed in the younger age-groups and in those who, prior to treatment, had had the more severe types of rheumatic episodes." There was a "higher incidence and greater danger of recurrences in those who previously suffered most frequent or severe attacks of rheumatic carditis".

W. G. Wyllie.

Some Public Health Aspects of Rheumatic Fever. Including the Present Status of Organized Efforts to Control its Effects. WHEATLEY, G. M. (1947). *W. Va. med. J.* **43**, 57.

Some epidemiological factors related to the control of rheumatic fever—the risk of recurrence decreasing with lapse of time from the original attack and with increasing age, family susceptibility, geographical and seasonal variations—are reviewed. There has been a marked decrease in severity in recent years, as shown by a 38% decrease in mortality since 1938. Transference of the patient to a more favourable climate, tonsillectomy, and salicylate prophylaxis have failed to prevent recurrences. On the other hand prolonged administration of the sulphonamides has given some promising results in spite of its obvious dangers. The author stresses the need for organized medico-social action such as has already been started in one State and a few major cities in the U.S.A. Five aspects of a community rheumatic fever programme are outlined—case finding to determine the magnitude of the problem, a diagnostic service to identify the disease especially in schools, provision of care in hospitals, homes, and schools, education (both professional and lay), and research.

H. F. Turney.

Rheumatic Fever Following Athletic Trauma. [In English.] JOKL, E., and MELZER, L. (1947). *Acta med. orient.*, **6**, 9.

An Observation Concerning the Hands of Patients with Rheumatic Fever. [In English.] DREYFUSS, F. (1947). *Acta med. orient.*, **6**, 12.

Articular Rheumatism

(Rheumatoid Arthritis)

Blood Sugar Level following Intravenous Glucose in Rheumatoid Arthritis. FLYNN, J. E., and IRISH, O. J. (1946). *Science*, **104**, 344.

So far no satisfactory explanation has been given of the oft-repeated observation that, following the oral administration of glucose, patients with rheumatoid arthritis show a slower return of the blood-sugar level to the fasting figure than do normal subjects. This has been considered to be due to faulty intestinal absorption, disturbance of pancreatic function, circulatory abnormalities, and dysfunction.

To evaluate the part played by gastro-intestinal dysfunction and/or intestinal circulatory alterations, Soskin's intravenous glucose tolerance test was done on 64 patients with rheumatoid arthritis and on 60 normal subjects. Soskin's method is to inject intravenously 0·3 g. of dextrose per kilo of body weight in a 50% aqueous solution within a period of 3 to 5 minutes. A pre-injection fasting sample and venous blood samples taken 30 to 60 and 120 minutes after injection were assayed by the Somogyi method for the determination of the true blood-sugar level. Of the cases of rheumatoid arthritis, 8 (12·5%) returned to the fasting level within 60 minutes; in 42 (65·6%) a return to the fasting level in between 60 and 120 minutes took place; while in 14 (21·9%) the blood-sugar levels were higher than the pre-injection figure at the end of 120 minutes. Of the normal cases, 43 (71·7%) returned to the pre-injection level in 60 minutes; in 16 (26·7%) the blood sugar returned to the pre-injection levels in between 60 and 120 minutes. In 1 subject the blood sugar was still elevated at the end of 120 minutes.

In Soskin's report (*Clinics*, 1943, **1**, 1286) the blood-sugar level of all the 30 normal controls returned to the pre-injection figure within 60 minutes after the intravenous administration of the glucose, whereas somewhat more than 25% of the author's normal controls failed to return within 60 minutes. This lack of agreement in no way detracts from the present study, since the intravenous glucose tolerance test was used primarily to evaluate the part played by intestinal dysfunction. Soskin further points out that the important factor is the time interval required for the return of the blood-sugar level to the pre-injection figure rather than the maximum height of the blood-sugar level. In view of the fact that the intravenous glucose tolerance test showed that the blood-sugar level fell more slowly in 87·5% of patients with rheumatoid arthritis than in 71·7% of normal controls, it can be concluded that intestinal dysfunction plays no part in the altered glucose tolerance found in the former.

In order to evaluate the possibility of the

altered glucose tolerance resulting from a difference in the amount of glucose lost in the urine, quantitative urinary glucose determinations were made on the 64 rheumatoid cases and the 60 normal controls. The difference between the 2-hour mean total urinary output of glucose of the rheumatoid patients (0·516) and of the normal controls (0·600) amounted to only 0·084 per 100 ml. of urine—obviously an amount too small to be significant. The possibility of the altered glucose tolerance in rheumatoid patients resulting from a diminution of peripheral glycogen deposits as a result of muscular atrophy was considered. The intravenous glucose tolerance test was done on 19 patients convalescing from severe poliomyelitis, all of whom had marked atrophy of at least three limbs. For a reason which is not apparent, the glucose tolerance curve for the poliomyelitis cases fell below that of both the normal and the rheumatoid groups. It is therefore obvious that the diminution of peripheral glycogen depots does not explain the alteration in the glucose tolerance found in rheumatoid subjects. With regard to the suggestion that pancreatic insufficiency affords an explanation of the altered glucose tolerance, Soskin has shown that there is a hepatic homeostatic control which supplies glucose to the blood stream when the blood-sugar level drops below a certain point. This equilibrium is affected by certain endocrine glands notably the pancreas, anterior lobe of the hypophysis, the thyroid, and the adrenal cortex. Hence hormonal influences affecting the hepatic homeostatic control of the blood-sugar level could account for the alteration in the glucose tolerance. The available data do not, however, permit evaluation of the role of these extrahepatic factors.

M. B. Ray.

Rheumatoid Arthritis. IV. Hemolytic Streptococcus Precipitin Reactions. WALLIS, A. D. (1947). *Amer. J. med. Sci.*, **213**, 87.

As a result of this work the author concludes that it is unlikely that the sera of patients with rheumatoid arthritis contain a genuine excess of haemolytic streptococcus precipitins. The antigens employed in the precipitin reactions were: (1) extracts made by Lancefield's method from haemolytic streptococci of groups A, B, C, D, E, F, and G, and (2) the C-carbohydrate substance characteristic of group A. The sera were obtained from patients with typical rheumatoid arthritis and from non-arthritic individuals free from recent streptococcal infection.

In the tests with the crude extracts obtained by Lancefield's method each antigen was used in amounts of 0·2 and 0·05 ml. These volumes were made up to 0·4 ml. with physiological saline. The saline control tube contained 0·4 ml. of saline without antigen, and 0·1 ml. of serum was added to each tube. The tubes were incubated in a water-bath at 37° C. for 2 hours, refrigerated overnight, centrifuged at 1,700 r.p.m. for 10 minutes, and examined. Where the C substance was used the antigen dilutions were 2×10^{-5} and 2×10^{-6}; otherwise the method was the same as for crude extracts, but prolonged observation with special visual aids was substituted for centrifugation.

Sera from 30 cases of arthritis did not precipitate antigens from crude extracts of streptococci of groups B, C, D, E, and F if the saline control was frankly negative. When, however, the control was positive, reactions with these extracts not only tended to be positive but often showed stronger precipitation than the control. In explanation of these findings the author considers it probable that the precipitation of serum of arthritic persons by saline may be enhanced by non-specific adsorption of a heterologous antigen. A high incidence of positive reactions between crude extracts of streptococci of group G and sera was considered of little significance, in view of the frequency of positive reactions between these extracts and sera from patients without arthritis.

While some sera from non-arthritic persons had a greater ability to precipitate an extract of group A streptococci than some sera from arthritic persons, the latter generally had more potency in this respect than the former, even when the saline control tube gave a negative result. However, the author has previously brought forward evidence (*Amer. J. med. Sci.*, 1946, **212**, 718), indicating that sera from patients with rheumatoid arthritis have the ability to enhance the action of normally present precipitins for a somatic carbohydrate of the pneumococcus; the occurrence of these precipitins in normal serum is attributable to the frequent presence of the pneumococcus in normal human throats. He considers that, similarly, group A haemolytic streptococcus precipitins present in normal sera and sera from arthritic persons may be enhanced in the latter.

With purified C-substance of group A the discrepancy between the two types of sera was greater than when the crude extract was used, precipitation occurring much less often with normal sera, but positive reactions with sera from arthritic persons were usually accompanied by a positive reaction in the saline control. In this case, where normal precipitins are feeble, the author is of opinion that both factors cited above, enhancement of action of normally present antibodies and non-specific antigen adsorption, may be active.

T. D. M. Martin.

Basophilic Stippling of the Red Corpuscles with Special Reference to its Occurrence during Chrysotherapy. PARR, L. J. A., and SHIPTON, E. A. (1947). *Med. J. Aust.*, **1**, 193.

The literature on basophilic stippling of red cells is reviewed at some length. Twenty patients taken at random from a series undergoing chrysotherapy were examined for stippled

cells. Films were collected and stained within a few hours of collection. Leishman's stain was used, but the film was left more blue than is usual. The stippled-cell count, according to the table, varied from 200 to 6,500 per million red cells. It is suggested that a high stippled-cell count indicates a toxic reaction to the drug.

[The stippled-cell count seems to have been performed only once on each patient and at a variable time after the institution of gold treatment. No control figures are quoted. It is not possible, therefore, to judge whether the basophilic stippling was due to the disease, to the drug, or to both.] *John F. Loutit.*

Three Cases of the Felty Syndrome. [In English.] YTREHUS (1947). *Acta med. Scand.*, **126**, 437.

Three cases of the Felty syndrome—polyarthritis, splenomegaly, and leucopenia—are described. Granulocytopenia was a marked feature in all, and there was almost complete agranulocytosis during exacerbations of the disease. In two of the cases sepsis was prominent. The author regards granulocytopenia as the essential feature of the syndrome and attributes it to an alteration in splenic function. He suggests that a common undetermined agent is the cause of both the splenic dysfunction and the polyarthritis.

H. F. Turney.

Still's Disease and Purpura Rheumatica. (Morbo di Still e peliosi reumatica.) FOFFANI, G. (1947). *Arch. Sci. med.*, **83**, 148.

In a case of Still's disease administration of sulphonamides was followed on three separate occasions by purpura, both cutaneous and abdominal. After the third attempt at treatment the purpura recurred on several occasions without any apparent cause. During each exacerbation the joint pains disappeared, returning when the purpura ceased. The condition of the joints continued to improve independently of these attacks. The purpura was accompanied by erythrocytosis and a relative increase in platelets. Ten months after the last purpuric episode the joint condition appeared to be quiescent, residual ankylosis existing in two joints. *J. G. Jamieson.*

Mobilization of Metacarpophalangeal Joints. Arthroplasty and Capsulotomy. FOWLER, S. B. (1947). *J. Bone Jt. Surg.*, **29**, 193.

The procedures of arthroplasty and capsulotomy for the mobilization of metacarpophalangeal joints are described. Arthroplasty is not advised in the case of the thumb or for digits which are anaesthetic, deformed, or lacking flexor tendons. A joint space of about 1 cm. is obtained mainly at the expense of the proximal phalanx. The metacarpal head is left broad and flat laterally and tapered anteroposteriorly; a fascial flap is interposed. Capsulotomy (really capsulectomy) is indicated for joints stiff in extension if the surfaces are intact and cannot be mobilized by physical therapy and traction. Frequently it forms part of a major procedure such as nerve suture or tendon transplantation. An incision is made on each side of the joint. The extensor expansion is split lateral to the extensor tendon and the collateral ligament completely removed. If the interphalangeal joints extend when the metacarpo-carpal joint is flexed, adhesion exists in the extensor tendon and must be corrected. The phalanx must glide around the anterior surface of the metacarpo-carpal head and not open like a book; this latter movement is due to an adherent anterior capsule and must be corrected by stripping. Full correction is maintained for 3 weeks, after which removable traction is employed for a month. Sixteen arthroplastes and over 100 capsulotomies have been performed. It is claimed that the procedures are relatively simple and provide useful joints unless there are too many other pathological changes.

[This important article by one of the Bunnell school should be read by all interested in the surgery of the hand. Many details of value are discussed.] *Norman Capener.*

(Spondylitis)

Rheumatoid Spondylitis: Its General Features and Management. BOLAND, E. W. (1946). *Calif. Med.*, **65**, 1.

Statistics of the incidence of spondylitis in service personnel show that 1,084 cases were seen in one two-year period, these comprising 18·1% of admissions of all types of rheumatism and nearly equalling the total number of cases of rheumatoid arthritis. Between 18 and 25% of cases were associated with peripheral rheumatoid arthritis, and the author, whilst recognizing that this is not a universal view, believes the disease to be merely rheumatoid arthritis of the spine. In 42% of 50 cases cerebrospinal fluid investigations revealed a raised protein content ranging from 45 to 105 mg. per 100 ml.; this rise in protein appeared to be related to the severity of the disease. A controlled study of treatment in a further 75 cases confirmed the value of deep *x*-ray therapy in early cases.

[This article, essentially clinical in nature, has as its aim a desire for earlier diagnosis and treatment of the disease. It would repay study in the original.] *D. P. Nicholson.*

Rheumatoid Spondylitis: Correlation of Clinical and Roentgenographic Features. BOLAND, E. W., and SHEBESTA, E. M. (1946). *Radiology*, **47**, 551.

A correlation of the clinical and roentgenographic features of the disease, its degree, severity, and rate of progress, are of value in arranging appropriate treatment. Radio-

graphic changes are seen usually in the sacro-iliac joints. The first changes consist of subchondral bony sclerosis and/or spotty demineralization, most often located in the juxta-articular portion of the ilium, in the caudal third. Later, similar changes appear in the juxta-articular portion of the sacrum. Involvement is usually bilateral, but not always symmetrical. Progression of the disease is associated with demineralization and bony condensation to a varying degree. The sacro-iliac joints at first appear blurred and the margins indistinct; the joint space may seem to be widened or narrowed; gradual ankylosis occurs and the subchondral sclerosis fades. Less frequent are changes in the lumbar, thoracic, and cervical spine, where calcification of the ligaments shows first at the thoraco-lumbar junction and progresses to the typical bamboo spine. *X*-ray of the apophyseal joints is technically difficult and of little value.

A correlation of clinical and radiographic findings was undertaken in 50 soldiers. The severity was gauged by the rapidity of progression of the disease, the amount of constitutional reaction, the degree of disability, the erythrocyte sedimentation rate, and the degree of anaemia; 27 cases were classified as mild, 20 as moderate, and 3 as severe. The average duration of symptoms was 4·4 years. Clinically there were signs of involvement of the sacro-iliac joints alone in 9; of sacro-iliac and lumbar spine in 21; of sacro-iliac and thoracic spine in 2; of sacro-iliac, lumbar, and thoracic spine in 13; of sacro-iliac, lumbar, and cervical spine in 1; and of all spinal segments in 4. All cases were *x*-rayed and the findings correlated. In general the severity of the disease was reflected in the changes seen in the sacro-iliac joints. The time interval before ankylosis of these joints occurred was extremely variable. Calcification or ossification of the paravertebral ligaments was a relatively late manifestation. Nine of the 50 cases showed changes in the apophyseal joints, but again this was not an early feature. Clinically, signs of involvement of sections of the spine preceded manifest radiographic changes. Two-thirds of the cases studied were more extensive clinically than radiologically. In deep *x*-ray therapy it is important to irradiate those areas which are judged to be involved clinically. Secondary changes in the muscles and ligaments are an important cause of pain and disability, as in rheumatoid arthritis, and this explains the discrepancy between clinical and radiological findings.

[The incidence of peripheral joints involvement is given as 25 to 30%. It is not stated whether this is a clinical or radiological finding, but it does not agree with the figure of 18 to 25% given in a comparable article (see above abstract). Reliable statistics on this point would be of interest.] *D. P. Nicholson.*

(Miscellaneous)

A Case of a Hitherto Undescribed Lipoidosis Simulating Rheumatoid Arthritis. GRAHAM, G., and STANSFELD, A. G. (1946). *J. Path. Bact.*, **58**, 545.

An unusual case clinically resembling a case of rheumatoid arthritis is described; it differs from other recorded cases of lipoidosis involving bones, joints, and muscles. A Gentile of 20 developed symmetrical pain, swelling, and fixation of fingers and wrists. Larger joints were affected later. Subcutaneous nodules appeared on scalp and face, and around joints and on the back; all the larger ones were symmetrical. Blood cholesterol was not raised. Histologically the nodules appeared to be typical xanthomata, but foam cells were negative to fat, mucin, and glycogen tests. Loosening of all teeth occurred; heat caused the appearance of fresh skin nodules; there were vitamin C retention and hyperkeratosis of thighs. Massive growth of the axillary nodule was followed by ulceration; severe muscular weakness was present, but no anaemia. The patient died after 3 years.

Post-mortem examination showed xanthomatous erosion of bone in relation to the swollen joints; the axillary tumour was sarcomatous and neuritic, but there were no metastases. Muscles (skeletal only) were pale and swollen, with lipoid degeneration of fibres and presence of xanthoma cells within the fibres. A positive reaction for neutral fat was given by some of the droplets and some xanthoma cells—the only mesenchymal tissue in which a sudanophil reaction was obtained. The reticulo-endothelial system was virtually unaffected, but the femur marrow showed gelatinous degeneration. The endocrines were normal. *A. C. Lendrum.*

Treatment of Chronic Rheumatism with Organic Salts of Copper. (Le traitement des rhumatismes chroniques par les sels organiques de cuivre.) FORESTIER, J., and CERTONCINY, A. (1946). *Presse méd.*, **54**, 884.

Since 1942, following previous German observations, the authors have conducted therapeutic tests at Aix-les-Bains of organic copper compounds in chronic rheumatic diseases. In their first series of 44 cases, published in 1944, there was a very favourable response in 20% and moderate improvement in 35%. The dose of copper in this series varied from 0·01 to 0·10 g., and the total quantity in one course from 0·6 to 1·5 g. The percentage of successful results increased with the higher doses used in the second series of 50 cases, now reported. Usually 0·25 g. has been given twice weekly, and the total quantity in one course has been 2·5, 3, 4, or even 5 g. An interval of 1 month has been allowed

between the first and second courses, and of 2 to 3 months between subsequent courses.

Attention is directed to the use of this copper compound in a syndrome of chronic polyarticular hydrarthrosis, which the authors consider to be a distinct entity; multiple joint effusions occur without synovial thickening and with little pain or disability, but have proved very refractory hitherto to all therapeutic methods. Effusion completely disappeared in 3 out of 5 cases. No toxic reactions occurred. *Kenneth Stone.*

A Surgical Procedure for the Painful Arthritic Hand. KESTLER, O. C. (1946). *Bull. Hosp. Jt. Dis.*, 7, 114.

An arthroplasty operation for cases of painful arthritis of the metacarpo-phalangeal joint, with or without deformity, is described. It is most applicable in cases which have not responded to conservative treatment, especially cases of rheumatoid arthritis which have developed marked ulnar deviation and dislocation of the metacarpo-phalangeal joint. A longitudinal incision is made between the joints if two adjacent joints are affected, or a curved transverse incision if all the joints are to be treated. The head and a portion of the neck of the bone are excised; as the bone is soft, it is removed with cutting scissors. A pseudo-arthrosis is formed and the capsule is sutured. After operation a compression bandage is used with the fingers in full flexion, and movements are started on the second day.

[The post-operative results are described as good and the procedure seems worth a trial. A similar operation has been used for many years on the foot with success.] *K. H. Pridie.*

Non-Articular Rheumatism

Psoriatic Rheumatism. (Reumatismo Psoriasico.) ROSSO, R. J. (1947). *Rev. argent. Reum.*, 11, 260.

Various theories on the causation of psoriatic rheumatism are reviewed. The author favours an infective cause acting through an allergic mechanism; the most important single organism responsible would be a streptococcus. Estimates of the incidence of the skin and joint lesions in combination vary greatly. The age incidence is over twenty and highest at 40 to 45, with slight preponderance in males. The skin lesions usually precede the joint lesions, and exacerbations of both types tend to occur together. The psoriasis may be of all types, and the nail lesions, producing longitudinal fissures, transverse striae, and punctate depressions, are stressed. The author describes separately the various forms of arthritis occurring with psoriasis—the "forme fruste", with myalgia and neuralgia; typical chronic progressive rheumatoid arthritis, indistinguishable from the form without skin lesions; subacute and chronic monarticular forms; recurrent or chronic hydrarthroses; periarticular form; acute generalized form; ankylosing spondylitis.

Blood chemical analysis reveals no constant changes but cell changes, such as leucocytosis with granulocytosis and sometimes mononucleosis or eosinophilia, are usual. Estimation of the erythrocyte sedimentation rate has diagnostic, prognostic, and therapeutic value. Diagnosis may have to be made from rheumatic fever, particularly by the absence of cardiac lesions and the failure to respond to salicylates; from osteo-arthritis; from infective arthritis; from keratodermia blenorrhagica when accompanied by arthritis; from Still's disease; from syphilis and tabes. Prognosis is difficult but on the whole poor. Treatment recommended is on the usual lines and, for the skin lesion particularly, on the whole unsatisfactory. Parenteral iodine, in inorganic and organic forms (for instance, as "lipiodol", 1 or 2 ml. intramuscularly every 48 hours), gold (up to a total of 2 or 2·5 g. in a course), colloidal sulphur, and tuberculin treatments are also described. The author cautions against using very active remedies for the skin lesions in view of the danger of exfoliative erythrodermia, and he recommends 5 to 10% ichthyol in mineral oil.

Three full case reports are given.

L. P. R. Fourman.

Sciatica. (Ciáticas). ZAMORA, R. L. (1946). *Sem. med.*, 53, 643.

The successful treatment of sciatica must depend on a painstaking search for the aetiological agent. A historical survey of the classifications of Landouzy, Déjerine, and others is made, with a short discussion of points in differential diagnosis of radiculitis, funiculitis, plexitis, and neuritis. In the author's view, herniation of an intervertebral disc is a rare cause of sciatica and there is a tendency at present to make the diagnosis too often. A number of cases of sciatica of different aetiology are discussed and the standard treatment described.

S. S. B. Gilder.

Lumbago and Sciatica as Industrial Accidents. (Lumbago y ciaticas como accidentes del trabajo.) Bard, L. (1947). *Med. Méx.*, 26, 47.

Sciatica and Lumbago due to Rupture of the Intervertebral Disk. (Ciática y lumbociática por lesión del disco intervertebral.) CARLOS ETHCHEGOYEN, J. (1947). *Prensa méd. argent.*, 34, 583.

Interstitial Neuritis and the Pressure Theory of Pain: a Critical Review and a Reflex Hypothesis. KELLY, M. (1946). *Med. J. Austral.*, 2, 325.

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